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(54) Title: PROCESS FOR COATING A MATERIAL SURFACE

(57) Abstract: The invention relates to a process for coating a material surface comprising the steps of: (a) reacting the material surface with a compound of formula (I), wherein the variables are as defined in the claims; (b) reacting the so modified surface with a functional polymerization initiator having a functional group that is co-reactive to L_2 or $L_{2'}$; and (c) applying one or more different ethylenically unsaturated hydrophilic monomers or macromonomers to the bulk material surface obtainable according to step (b) and polymerizing said macromonomers, thereby providing a preferably hydrophilic surface coating onto the material surface. Composite materials obtainable according to the process of the invention have desirable characteristics regarding adherence to the substrate, durability, hydropholicity, wettability, biocompatibility and permeability and are thus useful for the manufacture of biomedical articles such as ophthalmic devices.

Process for coating a material surface

The present invention relates to a process for coating articles, wherein the coating comprises a polymer having desirable characteristics regarding adherence to the substrate, durability, softness, hydrophilicity, lubricity, wettability, biocompatibility and permeability. More particular, the present invention relates to a process for coating an article, such as a biomedical material or article, especially a contact lens including an extended-wear contact lens, wherein at least a part of the coating comprises a polymer having a "bottle-brush" type structure composed of tethered "hairy" chains. The inventive coatings are obtainable by grafting specific ethylenically unsaturated macromonomers onto the surface of a substrate, which has been previously provided with initiator groups.

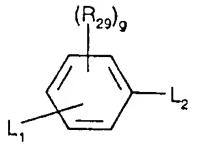
A variety of different types of processes for preparing hydrophilic polymeric coatings on an "inert" hydrophobic substrate have been disclosed in the prior art. For example, WO 99/57581 discloses to first of all provide the article surface with covalently bound photoinitiator molecules, coating the modified surface with a layer of a polymerizable macromonomer and then subjecting it to a heat or radiation treatment whereby the macromonomer is graft polymerized thus forming the novel article surface. The covalent binding of the photoinitiator molecules to the article surface is created by first subjecting the article surface to a plasma treatment thereby providing the surface with functional groups, and then reacting said functional groups with co-reactive groups of a functional photoinitiator.

A plasma treatment requires a considerable investment in equipment and is furthermore difficult to be integrated in an automated production process. For example, a plasma treatment requires that the article to be treated is dry before exposure to the plasma. Thus, a polymeric article such as a contact lens that is wet from prior hydration or extraction must be dried previously, thereby adding time in the overall lens production process as well as imposing added costs of obtaining a drying equipment. Therefore, it would be highly desirable to modify the surface functionalization step of the process disclosed in WO 99/57581 such that the plasma treatment is avoided and replaced by a technique which is easy to perform with standard equipment and which is thus more feasible for an automated production process.

Surprisingly, it has now been found, that a large variety of articles may be readily functionalized by means of certain hetero-bifunctional compounds having a first highly reactive functional group, which is able to react with the "inert" article surface, and a second functional group for further covalent attachment of reactive molecules such as initiators, catalysts, polymers, enzymes and biocomponents.

The present invention therefore in one aspect relates to a process for coating a material surface comprising the steps of:

(a) reacting the material surface with a compound of formula



(1),

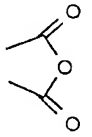
wherein R_{29} is C_1-C_4-alkyl, C_1-C_4-alkoxy, amino, hydroxy, sulfo, nitro, trifluoromethyl or halogen,

g is an integer from 0 to 2,

L_1 is a group, which functions as a triggerable precursor for carbene, nitrene or benzhydrol formation,

L_2 is amino, C_1-C_4-alkylamino, hydroxy, glycidyl, carboxy or a derivative thereof, isocyanato or isothiocyanato, or is a radical of formula

$$- [L_3]_h - (\text{spacer}) - L_2' \qquad (1a), \text{ or}$$

L_2 and R_{29} together form an anhydride radical  ;

L_2' is amino, C_1-C_4-alkylamino, hydroxy, carboxy or a derivative thereof, isocyanato, isothiocyanato, -O-glycidyl or $-O-C(O)-(CH_2)_{h1}-X_2$, wherein h1 is from 1 to 4 and X_2 is carboxy or a derivative thereof,

L_3 is –NH-, $-NC_1$-C_6-alkyl-, –O-, -C(O)O-, -C(O)NH-, -NHC(O)NH-, –NHC(O)O- or -OC(O)NH-;

(spacer) is linear or branched C_1-C_{200}-alkylene which may be substituted by hydroxy and/or interrupted by –O- except for C_1-alkyl, or is C_3-C_8-cycloalkylene, C_3-C_8-cycloalkylene-C_1-C_6-

alkylene, C_3-C_8-cycloalkylene-C_1-C_2-alkylene-C_3-C_8-cycloalkylene or C_1-C_6-alkylene-C_3-C_8-cycloalkylene-C_1-C_6-alkylene; and
h is the number 0 or 1;
(b) reacting the so modified surface with a functional polymerization initiator having a functional group that is co-reactive to L_2 or L_2'; and
(c) applying one or more different ethylenically unsaturated hydrophilic monomers or macromonomers to the bulk material surface obtainable according to step (b) and polymerizing said monomers or macromonomers, thereby providing a preferably hydrophilic surface coating onto the material surface.

Suitable materials to be coated according to the invention are, for example, natural or synthetic organic polymers, or laminates, composites or blends of said materials, in particular natural or synthetic organic polymers or modified biopolymers which are known in large number. Some examples of polymers are polyaddition and polycondensation polymers (polyurethanes, epoxy resins, polyethers, polyesters, polyamides and polyimides); vinyl polymers (polyacrylates, polymethacrylates, polyacrylamides, polymethacrylamides, polystyrene, polyethylene and halogenated derivatives thereof, polyvinyl acetate and polyacrylonitrile); or elastomers (silicones, polybutadiene and polyisoprene).

A preferred group of materials to be coated are those being conventionally used for the manufacture of biomedical devices, e.g. contact lenses, in particular contact lenses for extended wear, which are not hydrophilic per se. Such materials are known to the skilled artisan and may comprise for example polysiloxanes, perfluoroalkyl polyethers, fluorinated poly(meth)acrylates or equivalent fluorinated polymers derived e.g. from other polymerizable carboxylic acids, polyalkyl (meth)acrylates or equivalent alkylester polymers derived from other polymerizable carboxylic acids, or fluorinated polyolefines, such as fluorinated ethylene or propylene, for example tetrafluoroethylene, preferably in combination with specific dioxols, such as perfluoro-2,2-dimethyl-1,3-dioxol. Examples of suitable bulk materials are e.g. lotrafilcon A, neofocon, pasifocon, telefocon, silafocon, fluorsilfocon, paflufocon, elastofilcon, fluorofocon or teflon AF materials, such as teflon AF 1600 or teflon AF 2400 which are copolymers of about 63 to 73 mol % of perfluoro-2,2-dimethyl-1,3-dioxol and about 37 to 27 mol % of tetrafluoroethylene, or of about 80 to 90 mol % of perfluoro-2,2-dimethyl-1,3-dioxol and about 20 to 10 mol % of tetrafluoroethylene.

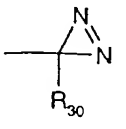
Another group of preferred materials to be coated are amphiphilic segmented copolymers comprising at least one hydrophobic segment and at least one hydrophilic segment which are linked through a bond or a bridge member. Examples are silicone hydrogels, for example those disclosed in PCT applications WO 96/31792 and WO 97/49740 which are herewith incorporated by reference.

A particular preferred group of materials to be coated comprises organic polymers selected from polyacrylates, polymethacrylates, polyacrylamides, poly(N,N-dimethylacrylamides), polymethacrylamides, polyvinyl acetates, polysiloxanes, perfluoroalkyl polyethers, fluorinated polyacrylates or -methacrylates and amphiphilic segmented copolymers comprising at least one hydrophobic segment, for example a polysiloxane or perfluoroalkyl polyether segment or a mixed polysiloxane/perfluoroalkyl polyether segment, and at least one hydrophilic segment, for example a polyoxazoline, poly(2-hydroxyethylmethacrylate), polyacrylamide, poly(N,N-dimethylacrylamide), polyvinylpyrrolidone polyacrylic or polymethacrylic acid segment or a copolymeric mixture of two or more of the underlying monomers.

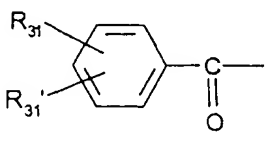
The material to be coated may also be any blood-contacting material conventionally used for the manufacture of renal dialysis membranes, blood storage bags, pacemaker leads or vascular grafts. For example, the material to be modified on its surface may be a polyurethane, polydimethylsiloxane, polytetrafluoroethylene, polyvinylchloride, Dacron™ or Silastic™ type polymer, or a composite made therefrom.

The form of the material to be coated may vary within wide limits. Examples are particles, granules, capsules, fibres, tubes, films or membranes, preferably moldings of all kinds such as ophthalmic moldings, for example intraocular lenses, artificial cornea or in particular contact lenses.

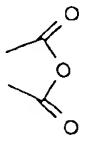
L_1 in formula (1) is, for example, a group of formula



(2a), -N_3 (2b) , or

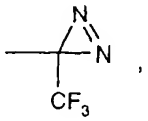
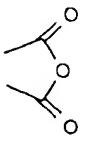


(2c)

wherein R_{30} is an electron-withdrawing substituent, for example fluorinated C_1-C_6-alkyl, such as a radical $-C_2F_5$ or preferably a radical $-CF_3$, and R_{31} and R_{31}' are each independently of the other hydrogen, amino, hydroxy, glycidyl, $-O-(CH_2)_{2-4}-O$-glycidyl, carboxy, a carboxy derivative or isocyanato, or R_{31} and R_{31}' together are an anhydride radical  .

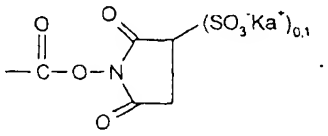
R_{29} is preferably C_1-C_4-alkoxy, nitro, C_1-C_4-alkyl, hydroxy, amino or sulfo. The variable g is, for example, 1 or preferably 0.

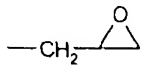
R_{31} is preferably hydrogen or amino and R_{31}' is preferably hydrogen; a further preferred embodiment relates to a radical of formula (2c), wherein R_{31} and R_{31}' together are an anhydride radical as outlined above.

One group of suitable radicals of formula (1) are those wherein L_1 is a group  , and g is 0. A further group of suitable radicals of formula (1) are those wherein L_1 is a group $-N_3$, and g is 1 or preferably 0. Still a further group of suitable radicals of formula (1) are those, wherein L_1 is a group of formula (2c) above, and wherein R_{31} is hydrogen or amino and R_{31}' is hydrogen, or R_{31} and R_{31}' together are an anhydride radical  .

Throughout the application the terms carboxy derivative, a derivative of carboxy and the like are to be understood as meaning, for example, a lactone, a carboxylic acid anhydride, halide, amide or ester, for example $-C(O)Cl$, $-C(O)NH_2$, $-C(O)C_1$-C_6-alkyl, -C(O)-phenyl or in particular an activated ester such as carboxy having been reacted with an activating agent, for example with N-hydroxy succinimide (NHS) or sulfo-N-hydroxy succinimide. A

particularly preferred carboxy derivative is an activated ester of formula



The term glycidyl means a radical  . The bivalent radcals L_3 are always to be understood that the left bond is directed to the phenyl ring and the right bond is directed to the (spacer) radical.

According to one preferred embodiment of the invention, L_2 is amino, isocyanato, isothiocyanato, carboxy or a derivative thereof, and in particular amino, isocyanato, carboxy, or an activated carboxylic acid ester as mentioned above.

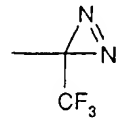
L_3 in formula (1a) is preferably a bivalent group –O-, –NH-, -C(O)O-, -C(O)NH- or -NHC(O)NH-, and is most preferably a radical –NH-, -C(O)O- or –C(O)NH-. h is preferably the number 1.

(spacer) in formula (1a) is preferably linear or branched, optional hydroxy-substituted, C_1-C_{24}-alkylene or C_4-C_{160}-alkylene which is interrupted by –O-, more preferably C_1-C_{16}-alkylene or C_8-C_{160}-alkylene which is interrupted by -O- and most preferably C_2-C_{12}-alkylene or –(alk')-O-$(CH_2CH_2O)_{18\text{-}160}$-(alk')-, wherein (alk') is, for example, C_1-C_6-alkylene, preferably C_1-C_4-alkylene, more preferably C_1-C_3-alkylene and in particular 1,2-ethylene. If (spacer) is a cycloalkylene or mixed alkylene/cycloalkylene radical, the meanings and preferences given below for R_{33} apply.

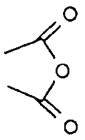
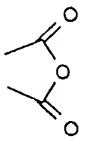
L_2' is preferably amino, isocyanato, carboxy, a carboxy derivative, or a radical -O-C(O)-$(CH_2)_2$-X_2, wherein X_2 is carboxy or a derivative thereof. Particularly preferred meanings of L_2' are amino, carboxy and an activated carboxylic acid ester as mentioned above.

A further preferred embodiment of the invention relates to the use of a compound of formula (1), wherein L_2 is a radical of formula (1a), L_3 is -NH-, -C(O)O- or –C(O)NH-, h is 1, (spacer) is linear C_2-C_{12}-alkylene or –(C_2-C_3-alkylene)-O-$(CH_2CH_2O)_{18\text{-}160}$-($C_2$-$C_3$-alkylene)-,

and L_2' is carboxy, a carboxy derivative or a radical -O-C(O)-$(CH_2)_2$-X_2, wherein X_2 is carboxy or an activated carboxylic acid ester as mentioned above.

Preferably, L_1 is a group of formula  , g is 0, and L_2 is carboxy, a carboxy derivative, or a radical of formula (1a) above, wherein the above-given meanings and preferences apply.

According to another preferred embodiment, L_1 is a group $-N_3$, g is 1 or preferably 0, R_{29} is methyl, methoxy, hydroxy or nitro, and L_2 is amino, carboxy, a carboxy derivative, isocyanato, isothiocyanato or a radical of formula (1a) above, wherein the above-mentioned meanings and preferences apply, in particular amino.

According to still a further preferred embodiment, L_1 is a radical of formula (2c) above, wherein R_{31} is hydrogen or amino and R_{31}' is hydrogen, or R_{31} and R_{31}' together are a radical  and L_2 is amino, g is 0 or 1 and R_{29} is amino, or L_2 and R_{29} together are a radical  .

The compounds of formula (1) may be applied to the material surface according to processes known per se. For example, the bulk material is immersed in a solution of a compound of formula (1), or a layer of a compound of formula (1) is first of all deposited on the bulk material surface to be modified, for example, by dipping, spraying, printing, spreading, pouring, rolling, spin coating or vacuum vapor deposition, with dipping or spraying being preferred. Most preferably, a solution comprising one or more different compounds of the formula (1) is sprayed onto the bulk material surface, which may be dry

or preferably wet. The compound of formula (1) may be applied to the material surface in one cycle or in repeated cycles.

Suitable solvents useful as solvents of the compounds of formula (1) are, for example, water, C_1-C_4-alkanols such as methanol, ethanol or iso-propanol, nitriles such as acetonitrile, tetrahydrofurane (THF), aqueous solutions comprising an alkanol, THF or the like, ketones, for example acetone or methylethyl ketone, and also hydrocarbons, for example halogenated hydrocarbons such as methylene chloride or chloroform. The concentration of the compound of formula (1) in the spray solution depends on the specific compound used but is in general in the range of from 0.1 to 100 g/l, preferably 0.5 to 50 g/l, more preferably 0.5 to 25 g/l and in particular 1 to 10 g/l.

The fixation of the compounds of formula (1) on the bulk material surface then may be initiated, for example, by irradiation, particularly by irradiation with UV or visible light. Suitable light sources for the irradiation are known to the artisan and comprise for example mercury lamps, high pressure mercury lamps, xenon lamps, carbon arc lamps or sunlight. Sensitizers may be used to shift the irradiation wavelength. In addition, a suitable filter may be used to limit the irradiation to a specific wavelength range. Preferably, the bulk material surface to which the compound(s) of formula (1) have been previously applied, is irradiated with light of a wavelength ≥250nm and preferably ≥300nm. The time period of irradiation is not critical but is usually in the range of up to 30 minutes, preferably from 10 secondes to 10 minutes, and more preferably from 15 seconds to 5 minutes, and particularly preferably from 20 seconds to 1 minute. The irradiation may be carried out under ambient conditions or in an atmosphere of inert gas. Masks can be used for the generation of specific surface patterns of functional groups. Following the fixation reaction, any non-covalently bound compounds can be removed, for example by treatment, e.g. extraction, with suitable solvents, for example water, C_1-C_4-alkanols, water/C_1-C_4-alkanol mixtures or acetonitrile.

Depending on the desired concentration of functional groups L_2 on the material surface, the above outlined process cycle, (i) contacting, i.e. spraying or dipping, the surface with the compound(s) of formula (1) and (ii) fixing the compound(s) of formula (1) on the surface, i.e. by irradiation, may be carried out once or, preferably, several times. For example, 1 to 100, preferably 1 to 50 and in particular 5 to 25, different layers of one or more compounds of formula (1) are added and fixed on the material surface.

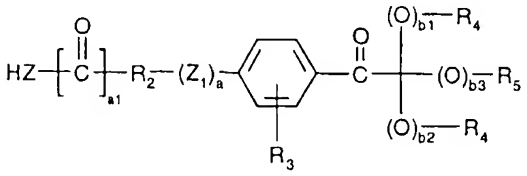
A polymerization initiator according to step (b) is typically one that is initiating a radical polymerization of ethylenically unsaturated compounds. The radical polymerization may be induced thermally, or preferably by irradiation.

Suitable thermal polymerization initiators are known to the skilled artisan and comprise for example peroxides, hydroperoxides, azo-bis(alkyl- or cycloalkylnitriles), persulfates, percarbonates or mixtures thereof. Examples are benzoylperoxide, tert.-butyl peroxide, di-tert.-butyl-diperoxyphthalate, tert.-butyl hydroperoxide, azo-bis(isobutyronitrile), 1,1'-azo-bis (1-cyclohexanecarbonitrile), 2,2'-azo-bis(2,4-dimethylvaleronitrile), 4,4'-azo-bis(4-cyano-valeric acid, 4,4'-azo-bis(4-cyano-n-pentanol) and the like. Initiators for the thermal polymerization are particularly functional initiators having an initiator part such as a peroxide, hydroperoxide, persulfate or azo group and in addition a functional group that is co-reactive with the functional groups L_2 of the modified material surface obtainable according to step (a). Suitable functional groups that are co-reactive with L_2 are, for example, a carboxy, amino, hydroxy, epoxy or isocyanato group. A particular preferred group of thermal initiators are azo-bis(C_2-C_{12}-alkane carboxylic acids) or azo-bis(C_2-C_{12}-alkanols) wherein the alkane moiety in each case may be further substituted, for example, by cyano.

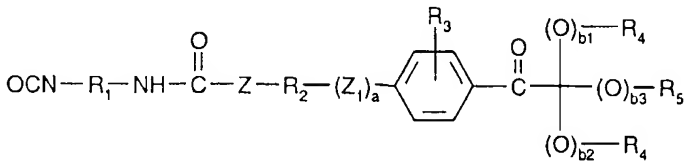
Initiators for the radiation-induced polymerization are particularly functional photoinitiators having a photoinitiator part and in addition a functional group that is co-reactive with the functional groups L_2 of the modified material surface obtainable according to step (a). The photoinitiator part may belong to different types, for example to the thioxanthone type and preferably to the benzoin type. Suitable functional groups that are co-reactive with L_2 are, for example, a carboxy, amino, hydroxy, epoxy or isocyanato group.

Preferred polymerization initiators for use in the present invention are the photoinitiators of formulae (I) and (Ia) as disclosed in US patent No. 5,527,925, those of the formula (I) as disclosed in PCT application WO 96/20919, or those of formulae II and III including formulae IIa-IIy and IIIg as disclosed in EP-A-0281941, particularly formulae IIb, IIi, IIm, IIn, IIp, IIr, IIs, IIx and IIIg therein. The respective portion of said three documents including the definitions and preferences given for the variables in said formulae are herewith included by reference.

The polymerization initiator moieties are preferably derived from a functional photoinitiator of the formula



(3a),



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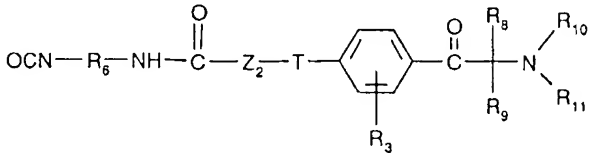
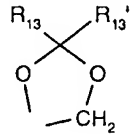
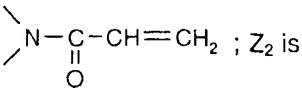


(3c),

wherein Z is bivalent -O-, -NH- or -NR_{12}-; Z_1 is -O-, -O-(O)C-, -C(O)-O- or -O-C(O)-O-; R_3 is H, C_1-C_{12}-alkyl, C_1-C_{12}-alkoxy or N-C_1-C_{12}-alkylamino; R_4 and R_5 are each independently of the other H, linear or branched C_1-C_8-alkyl, C_1-C_8-hydroxyalkyl or C_6-C_{10}-aryl, or the groups R_4-$(O)_{b1}$- and R_4-$(O)_{b2}$- together are -$(CH_2)_c$- wherein c is an integer from 3 to 5, or the groups R_4-$(O)_{b1}$-, R_4-$(O)_{b2}$- and R_5-$(O_1)_{b3}$- together are a radical of the formula



; R_2 is a direct bond or linear or branched C_1-C_8-alkylene that is unsubstituted or substituted by -OH and/or is uninterrupted or interrupted by one or more groups -O-, -O-C(O)- or -O-C(O)-O-; R_1 is branched C_3-C_{18}-alkylene, unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_6-C_{10}-arylene, or unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_7-C_{18}-aralkylene, unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_3-C_8-cycloalkylene, unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_3-C_8-cycloalkylene-C_yH_{2y}- or unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted -C_yH_{2y}-(C_3-C_8-cycloalkylene)-C_yH_{2y}- wherein y is an integer from 1 to 6; R_6 independently has the same definitions as R_1 or is linear C_3-C_{18}-alkylene; R_{12} is linear or branched C_1-C_6-alkyl; T is

bivalent -O-, -NH-, -S-, C_1-C_8-alkylene or  ; Z_2 is a direct bond or

-O-$(CH_2)_d$- or –$(OCH_2CH_2)_d$- wherein d is an integer from 1 to 6 and the terminal CH_2 group of which is each linked to the adjacent T in formula (3c); R_8 is linear or branched C_1-C_8-alkyl, C_2-C_8-alkenyl or C_6-C_{10}-aryl-C_1-C_8-alkyl; R_9 independently of R_8 has the same definitions as R_8 or is C_6-C_{10}-aryl, or R_8 and R_9 together are -$(CH_2)_e$- wherein e is an integer from 2 to 6; R_{10} and R_{11} are each independently of the other linear or branched C_1-C_8-alkyl that may be substituted by C_1-C_4-alkoxy, or C_6-C_{10}-aryl-C_1-C_8-alkyl or C_2-C_8-alkenyl; or R_{10} and R_{11} together are -$(CH_2)_{f1}$-Z_3-$(CH_2)_{f2}$- wherein Z_3 is a direct bond, -O-, -S- or -NR_7-, and R_7 is H or C_1-C_8-alkyl and f1 and f2 are each independently of the other an integer from 2 to 4; R_{13} and R_{13}' are each independently of the other H, C_1-C_8-alkyl, C_3-C_8-cycloalkyl, benzyl or phenyl; and a, a1, b1, b2 and b3 are each independently of the other 0 or 1; subject to the provisos that b1 and b2 are each 0 when R_{15} is H; that the total of (b1+b2+b3) is not exceeding 2; and that a is 0 when R_{12} is a direct bond.

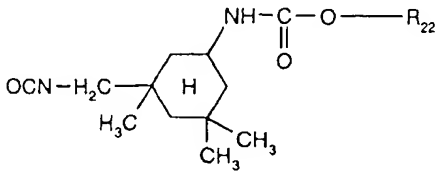
A preferred sub-group of compounds of formula (3a) or (3b) comprises those wherein, b1 and b2 are each 0; Z and Z_1 are each bivalent -O-; b3 is 0 or 1; R_4 is C_1-C_4-alkyl or phenyl, or both groups R_4 together are tetramethylene or pentamethylene; R_5 is C_1-C_4-alkyl or H, R_3 is hydrogen; a and a1 are each independently 0 or 1; R_2 is linear or branched C_2-C_4-alkylene, or is a direct bond, in which case a is 0; R_1 is branched C_5-C_{10}-alkylene, phenylene or phenylene substituted by from 1 to 3 methyl groups, benzylene or benzylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexyl-C_yH_{2y}- or -C_yH_{2y}-cyclohexyl-C_yH_{2y}- or cyclohexyl-C_yH_{2y}- or -C_yH_{2y}-cyclohexyl-C_yH_{2y}- substituted by from 1 to 3 methyl groups; and y is 1 or 2.

An especially preferred sub-group of compounds of formula (3a) or (3b) comprises those wherein, b1 and b2 are each 0, Z and Z_1 are each bivalent -O-, b3 is 0 or 1; R_4 is methyl or phenyl, or both groups R_4 together are pentamethylene; R_5 is methyl or H; R_3 is hydrogen; a is 1 and R_2 is ethylene, or a is 0 and R_2 is a direct bond; a1 is 0 or 1; and R_1 is branched C_6-C_{10}-alkylene, phenylene or phenylene substituted by from 1 to 3 methyl groups, benzylene or benzylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexyl-CH_2- or cyclohexyl-CH_2- substituted by from 1 to 3 methyl groups.

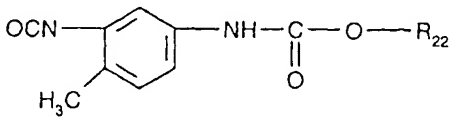
A preferred sub-group of compounds of formula (3c) comprises those wherein T is bivalent -O-, -NH-, -S- or $-(CH_2)_y-$ wherein y is an integer from 1 to 6; Z_2 is a direct bond or $-O-(CH_2)_y-$ wherein y is an integer from 1 to 6 and the terminal CH_2 group of which is linked to the adjacent T in formula (3c); R_3 is H, C_1-C_{12}-alkyl or C_1-C_{12}-alkoxy; R_8 is linear C_1-C_8-alkyl, C_2-C_8-alkenyl or C_6-C_{10}-aryl-C_1-C_8-alkyl; R_9 independently of R_8 has the same definitions as R_8 or is C_6-C_{10}-aryl, or R_8 and R_9 together are $-(CH_2)_e-$ wherein e is an integer from 2 to 6; R_{10} and R_{11} are each independently of the other linear or branched C_1-C_8-alkyl that may be substituted by C_1-C_4-alkoxy, or C_6-C_{10}-aryl-C_1-C_8-alkyl or C_2-C_8-alkenyl; or R_{10} and R_{11} together are $-(CH_2)_{f1}-Z_3-(CH_2)_{f2}-$ wherein Z_3 is a direct bond, -O-, -S- or $-NR_7-$, and R_7 is H or C_1-C_8-alkyl and f1 and f2 are each independently of the other an integer from 2 to 4; and R_6 is branched C_6-C_{10}-alkylene, phenylene or phenylene substituted by from 1 to 3 methyl groups, benzylene or benzylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexylene-CH_2- or cyclohexylene-CH_2- substituted by from 1 to 3 methyl groups.

An especially preferred sub-group of compounds of formula (3c) comprises those wherein T is bivalent -O-; Z_2 is $-O-(CH_2)_y-$ wherein y is an integer from 1 to 4 and the terminal CH_2 group of which is linked to the adjacent T in formula (3c); R_3 is H; R_8 is methyl, allyl, tolylmethyl or benzyl, R_9 is methyl, ethyl, benzyl or phenyl, or R_8 and R_9 together are pentamethylene, R_{10} and R_{11} are each independently of the other C_1-C_4-alkyl or R_{10} and R_{11} together are $-CH_2CH_2OCH_2CH_2-$, and R_6 is branched C_6-C_{10}-alkylene, phenylene or phenylene substituted by from 1 to 3 methyl groups, benzylene or benzylene substituted by from 1 to 3 methyl groups, cyclohexylene or cyclohexylene substituted by from 1 to 3 methyl groups, cyclohexylene-CH_2- or cyclohexylene-CH_2- substituted by from 1 to 3 methyl groups.

Some examples of especially preferred functional photoinitiators are the compounds of formulae

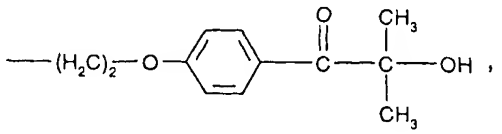


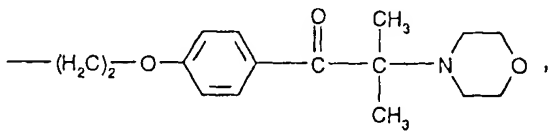
(3d1),

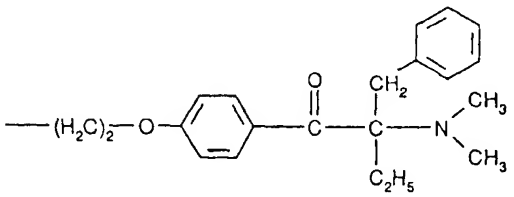


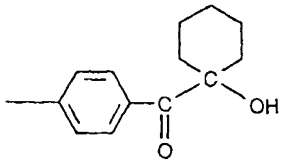
($3d_2$), or

$OCN\text{-}CH_2\text{-}C(CH_3)_2\text{-}CH_2\text{-}CH(CH_3)\text{-}CH_2\text{-}CH_2\text{-}NH\text{-}C(O)\text{-}O\text{-}R_{22}$ ($3d_3$),

wherein R_{22} is a radical  ,

 ,

 , or

 .

The reactions of radicals on the material surface that are derived from a compound of formula (1) having a carboxy, carboxy derivative, isocyanato or isothiocyanato group L_2 with a functional polymerisation initiator having an amino or hydroxy group, or vice versa, are well-known in the art and may be carried out as desribed in textbooks of organic chemistry. For example, the reaction of a radical derived from a compound of formula (1), wherein L_2 is an isocyanato or isothiocyanato group with an amino- or hydroxy-functionalized polymerisation initiator, or vice versa the reaction of an amino- or hydroxy group L_2 with an isocyanato or isothiocyanato functionalized polymerisation initiator, may be carried out in an inert organic solvent such as an optionally halogenated hydrocarbon, for example petroleum ether, methylcyclohexane, toluene, chloroform, methylene chloride and the like, or an ether, for example diethyl ether, tetrahydrofurane, dioxane, or a more polar solvent

such as DMSO, DMA, N-methylpyrrolidone or even a lower alcohol, at a temperature of from 0 to 100°C, preferably from 0 to 50°C and particularly preferably at room temperature, optionally in the presence of a catalyst, for example a tertiary amine such as triethylamine or tri-n-butylamine, 1,4-diazabicyclooctane, or a tin compound such as dibutyltin dilaurate or tin dioctanoate. It is advantageous to carry out the above reactions under an inert atmosphere, for example under a nitrogen or argon atmosphere.

In case that the radicals on the material surface are derived from a compound of formula (1) having a carboxy group L_2, the reaction of the carboxy group with an amino or hydroxy group functionalized photoinitiator, or vice versa the reaction of an amino or hydroxy group L_2 with a carboxy functionalized polymerisation initiator, may be carried out under the conditions that are customary for ester or amide formation, for example in an aprotic medium at a temperature from about room temperature to about 100°C. It is further preferred to carry out the esterification or amidation reaction in the presence of an activating agent, for example N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide (EDC), N-hydroxy succinimide (NHS), sulfo-N-hydroxy succinimide or N,N'-dicyclohexyl carbodiimide (DCC) or in the presence of an o-(benztriazole)- uronium salt such as o-(benztriazol-1-y-)-N,N,N,N-tetramethyluronium hexafluorophosphate. Most preferably, the carboxy group L_2 is previously converted to an activated ester using one of the above-mentioned activating agents, and the activated ester is then further reacted with the hydroxy or preferably amino groups of the surface.

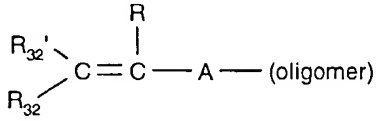
In a preferred embodiment of the invention, L_2 comprises amino, alkylamino or hydroxy, particularly amino, as reactive group and the co-reactive group of the polymerization initiator is an isocyanato group. A preferred polymerization initiator of this embodiment is a photoinitiator of the above formula (3b), (3c), ($3d_1$), ($3d_2$) or ($3d_3$).

According to another preferred embodiment of the invention, L_2 comprises carboxy, a carboxy derivative, isocyanato or isothiocyanato as reactive group, and the co-reactive group of the polymerization initiator is a hydroxy, amino, alkylamino or thiol group, particularly an amino group. A preferred polymerization initiator of this embodiment is a photoinitiator of the above formula (3a).

A hydrophilic monomer useful to provide the hydrophilic surface coating (c) on the initiator-modified bulk material surface is typical a monomer that yields as homopolymer a polymer that is water-soluble or can absorb at least 10 % by weight of water. Examples of preferred hydrophilic monomers are hydroxy-substituted C_2-C_4-alkyl acrylates and methacrylates, acrylamide, methacrylamide, N,N-di-C_1-C_4-alkyl acrylamides and methacrylamides, ethoxylated acrylates and methacrylates, hydroxy-substituted C_2-C_4-alkyl acrylamides and methacrylamides, hydroxy-substituted C_1-C_4-alkyl vinyl ethers, sodium ethylenesulfonate, sodium styrenesulfonate, 2-acrylamido-2-methylpropanesulfonic acid, N-vinylpyrrole, N-vinylsuccinimide, N-vinylpyrrolidone, 2- or 4-vinylpyridine, acrylic acid, methacrylic acid, amino- (the term "amino" also including quaternary ammonium), mono-C_1-C_4-alkylamino- or di-C_1-C_4-alkylamino-C_1-C_4-alkyl acrylates and methacrylates, allylalcohol and the like. Hydroxy-substituted or N,N-di-C_1-C_2-alkylamino-substituted C_2-C_4alkyl(meth)acrylates, five- to seven-membered N-vinyl lactams, N,N-di-C_1-C_4alkyl(meth)acrylamides and vinylically unsaturated carboxylic acids having a total of from 3 to 5 carbon atoms, for example, are preferred.

Examples of preferred hydrophilic vinylic monomers include hydroxyethyl methacrylate, hydroxyethyl acrylate, acrylamide, methacrylamide, N,N-dimethylacrylamide, allyl alcohol, N-vinylpyrrolidone, acrylic acid, methacrylic acid and N,N-dimethylaminoethyl methacrylate.

Preferably the hydrophilic surface coating (c) on the bulk material is obtained using a suitable macromonomer. A suitable macromonomer according to step (c) of the process of the invention is, for example, of formula



(4),

wherein R_{32} is hydrogen, C_1-C_6-alkyl or a radical -COOR';

R, R' and R_{32}' are each independently of the other hydrogen or C_1-C_6-alkyl;

A is a direct bond or is a radical of formula

$-C(O)-(A_1)_n-X-$ (5a) or

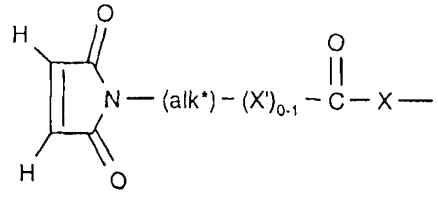
$-(A_2)_m-NH-C(O)-X-$ (5b); or

$-(A_2)_m-X-C(O)-$ (5c); or

$-C(O)-NH-C(O)-X-$ (5d); or

$-C(O)-X_1-(alk^*)-X-C(O)-$ (5e); or

A and R_{32}, together with the adjacent double bond, are a radical of formula



(5f),

A_1 is -O-C_2-C_{12}-alkylene which is unsubstituted or substituted by hydroxy, or is -O-C_2-C_{12}-alkylene-NH-C(O)- or -O-C_2-C_{12}-alkylene-O-C(O)-NH-R_{33}-NH-C(O)- or –NH-(Alk*)-C(O)-, wherein (Alk*) is C_1-C_6-alkylene and R_{33} is linear or branched C_1-C_{18}-alkylene or unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_6-C_{10}-arylene, C_7-C_{18}-aralkylene, C_6-C_{10}-arylene-C_1-C_2-alkylene-C_6-C_{10}-arylene, C_3-C_8-cycloalkylene, C_3-C_8-cycloalkylene-C_1-C_6-alkylene, C_3-C_8-cycloalkylene-C_1-C_2-alkylene-C_3-C_8-cycloalkylene or C_1-C_6-alkylene-C_3-C_8-cycloalkylene-C_1-C_6-alkylene ;

A_2 is C_1-C_8-alkylene; phenylene or benzylene;

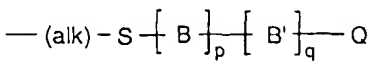
m and n are each independently of the other the number 0 or 1;

X, X_1 and X' are each independently of the other a bivalent group -O- or -NR", wherein R" is hydrogen or C_1-C_6-alkyl;

(alk*) is C_2-C_{12}-alkylene;

and (oligomer) denotes

(i) the radical of a telomer of formula



(6a),

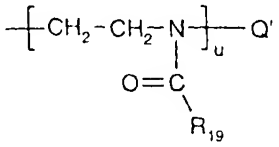
wherein (alk) is C_2-C_{12}-alkylene,

Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator,

p and q are each independently of another an integer from 0 to 350, wherein the total of (p+q) is an integer from 2 to 350,

and B and B' are each independently of the other a 1,2-ethylene radical derivable from a copolymerizable vinyl monomer by replacing the vinylic double bond by a single bond, at least one of the radicals B and B' being substituted by a hydrophilic substituent; or

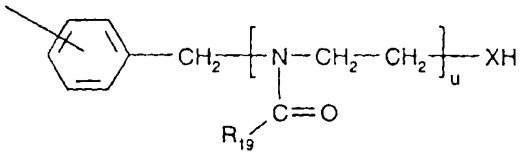
(ii) the radical of an oligomer of the formula



(6b),

wherein R_{19} is hydrogen or unsubstituted or hydroxy-substituted C_1-C_{12}-alkyl, u is an integer from 2 to 250 and Q' is a radical of a polymerization initiator; or

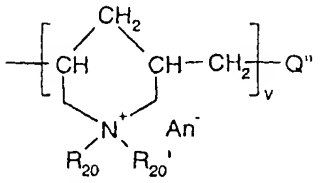
(iii) the radical of formula



(6b'),

wherein R_{19}, X and u are as defined above, or

(iv) the radical of an oligomer of formula



(6c),

wherein R_{20} and R_{20}' are each independently C_1-C_4-alkyl, An^- is an anion, v is an integer from 2 to 250, and Q'' is a monovalent group that is suitable to act as a polymerization chain-reaction terminator; or

(v) the radical of an oligopeptide of formula

$$-(CHR_{21}\text{-}C(O)\text{-}NH)_t\text{-}CHR_{21}\text{-}COOH \quad (6d) \text{ or}$$

$$-CHR_{21}\text{-}(NH\text{-}C(O)\text{-}CHR_{21})_t\text{-}NH_2 \quad (6d'),$$

wherein R_{21} is hydrogen or C_1-C_4-alkyl which is unsubstituted or substituted by hydroxy, carboxy, carbamoyl, amino, phenyl, o-, m- or p-hydroxyphenyl, imidazolyl, indolyl or a radical -NH-C(=NH)-NH_2 and t is an integer from 2 to 250, or the radical of an oligopeptide based on proline or hydroxyproline; or

(vi) the radical of a polyalkylene oxide of formula

$$-(alk^{\cdot\cdot}\text{-}O)_z\text{-}[CH_2\text{-}CH_2\text{-}O]_r\text{-}[CH_2\text{-}CH(CH_3)\text{-}O]_s\text{-}R_{34} \quad (6e),$$

wherein R_{34} is hydrogen or C_1-C_{24}-alkyl, ($alk^{\cdot\cdot}$) is C_2-C_4-alkylene, z is 0 or 1, r and s are each independently an integer from 0 to 250 and the total of (r+s) is from 2 to 250; or

(vii) the radical of an oligosaccharide;

subject to the provisos that

A is not a direct bond if (oligomer) is a radical of formula (6a);
A is a radical of formula (5a), (5b) or (5d) or A and R_{32}, together with the adjacent double bond, are a radical of formula (5f) if (oligomer) is a radical of formula (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide;
A is a direct bond if (oligomer) is a radical of formula (6b'); and
A is a radical of formula (5c) or (5e) if (oligomer) is a radical of formula (6d').

The following preferences apply to the variables contained in the definition of the macromonomer of formula (4):
R' is preferably hydrogen or C_1-C_4-alkyl, more preferably hydrogen or C_1-C_2-alkyl and particularly preferably hydrogen.
R_{32} is preferably hydrogen, methyl or carboxyl, and particularly preferably hydrogen.
R is preferably hydrogen or methyl.
X is preferably a bivalent group -O- or -NH-. X is particularly preferably the group -NH- if (oligomer) is a radical of formula (6a); (6c) or (6d), and is particularly preferably the group -O- if (oligomer) is a radical of formula (6b) or (6e) or is the radical of an oligosaccharide. X' is preferably -O- or -NH- and more preferably -NH-. X_1 is preferably -O- or -NH-.
R_{33} as alkylene is preferably a linear or branched C_3-C_{14}-alkylene radical, more preferably a linear or branched C_4-C_{12}alkylene radical and most preferably a linear or branched C_6-C_{10}-alkylene radical.

When R_{33} is arylene, it is, for example, naphthylene or especially phenylene, each of which may be substituted, for example, by C_1-C_4-alkyl or by C_1-C_4-alkoxy. Preferably, R_{33} as arylene is 1,3- or 1,4-phenylene that is unsubstituted or substituted by C_1-C_4-alkyl or by C_1-C_4-alkoxy in the ortho-position to at least one linkage site.

R_{33} as aralkylene is preferably naphthylalkylene and most preferably phenylalkylene. The alkylene group in aralkylene contains preferably from 1 to 12, more preferably from 1 to 6 and most preferably from 1 to 4 carbon atoms. Most preferably, the alkylene group in aralkylene is methylene or ethylene.

When R_{33} is cycloalkylene, it is preferably C_5-C_6-cycloalkylene and most preferably cyclohexylene that is unsubstituted or substituted by methyl.

If R_{33} is cycloalkylene-alkylene, it is preferably cyclopentylene-C_1-C_4-alkylene and especially cyclohexylene-C_1-C_4-alkylene, each unsubstituted or mono- or poly-substituted by C_1-C_4-alkyl, especially methyl. More preferably, the group cycloalkylene-alkylene is cyclohexylene-ethylene and, most preferably, cyclohexylene-methylene, each unsubstituted or substituted in the cyclohexylene radical by from 1 to 3 methyl groups.

When R_{33} is alkylene-cycloalkylene-alkylene, it is preferably C_1-C_4-alkylene-cyclopentylene-C_1-C_4-alkylene and especially C_1-C_4-alkylene-cyclohexylene-C_1-C_4-alkylene, each unsubstituted or mono- or poly-substituted by C_1-C_4-alkyl, especially methyl. More preferably, the group alkylene-cycloalkylene-alkylene is ethylene-cyclohexylene-ethylene and, most preferably, is methylene-cyclohexylene-methylene, each unsubstituted or substituted in the cyclohexylene radical by from 1 to 3 methyl groups.

R_{33} as C_3-C_8-cycloalkylene-C_1-C_2-alkylene-C_3-C_8-cycloalkylene or C_6-C_{10}-arylene-C_1-C_2-alkylene-C_6-C_{10}-arylene is preferably C_5-C_6-cycloalkylene-methylene-C_5-C_6-cycloalkylene or phenylene-methylene-phenylene, each of which may be unsubstituted or substituted in the cycloalkyl or phenyl ring by one or more methyl groups.

The radical R_{33} has a symmetrical or, preferably, an asymmetrical structure. A preferred group of radicals R_{11} comprises those, wherein R_{33} is linear or branched C_6-C_{10}alkylene; cyclohexylene-methylene or cyclohexylene-methylene-cyclohexylene each unsubstituted or substituted in the cyclohexyl moiety by from 1 to 3 methyl groups; or phenylene or phenylene-methylene-phenylene each unsubstituted or substituted in the phenyl moiety by methyl. The bivalent radical R_{33} is derived preferably from a diisocyanate and most preferably from a diisocyanate selected from the group isophorone diisocyanate (IPDI), toluylene-2,4-diisocyanate (TDI), 4,4'-methylenebis(cyclohexyl isocyanate), 1,6-diisocyanato-2,2,4-trimethyl-n-hexane (TMDI), methylenebis(phenyl isocyanate), methylenebis(cyclohexyl-4-isocyanate) and hexamethylene diisocyanate (HMDI).

Preferred meanings of A_1 are unsubstituted or hydroxy-substituted -O-C_2-C_8-alkylene or a radical -O-C_2-C_6-alkylene-NH-C(O)- and particularly -O-$(CH_2)_{2-4}$-, -O-CH_2-CH(OH)-CH_2- or a radical -O-$(CH_2)_{2-4}$-NH-C(O)-. A particularly preferred meaning of A_1 is the radical -O-$(CH_2)_2$-NH-C(O)-.

A_2 is preferably C_1-C_6-alkylene, phenylene or benzylene, more preferably C_1-C_4-alkylene and even more preferably C_1-C_2-alkylene.
n is an integer of 0 or preferably 1. m is preferably an integer of 1.
R_{32}' is preferably hydrogen or methyl and particularly preferably hydrogen.
In case that (oligomer) is a radical of formula (6a), (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide, is A preferably a radical of formula (5a) or (5b) and particularly preferably a radical of formula (5a), wherein the above given meanings and preferences apply for the variables contained therein.
A preferred group of hydrophilic macromonomers according to the invention comprises compounds of the above formula (4), wherein R is hydrogen or methyl, R_{32} is hydrogen, methyl or carboxyl, R_{32}' is hydrogen, A is a radical of the formula (5a) or (5b) and (oligomer) is a radical of formula (6a), (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide. An even more preferred group of hydrophilic macromonomers comprises compounds of the above formula (4), wherein R is hydrogen or methyl, R_{32} and R_{32}' are each hydrogen, A is a radical of the formula (5a) and (oligomer) is a radical of formula (6a). A further group of preferred macromonomers comprises compounds of formula (4), wherein A is a radical of formula (5e) above and (oligomer) is a radical of formula (6a).

(Alk*) is preferably methylene, ethylene or 1,1-dimethyl-methylene, in particular a radical $-CH_2-$ or $-C(CH_3)_2-$.

(alk) and (alk*) are each independently preferably C_2-C_8-alkylene, more preferably C_2-C_6-alkylene, even more preferably C_2-C_4-alkylene and particularly preferably 1,2-ethylene. The alkylene radicals (alk) and (alk*) may be branched or preferably linear alkylene radicals.

Q is for example hydrogen.

The total of (p+q) is preferably an integer from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50. In a preferred embodiment of the invention q is 0 and p is an integer from 2 to 250, preferably from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50.

Suitable hydrophilic substituents of the radicals B or B' may be non-ionic, anionic, cationic or zwitterionic substituents. Accordingly, the telomer chain of formula (5a) that contains monomer units B and/or B' may be a charged chain containing anionic, cationic and/or zwitterionic groups or may be an uncharged chain. In addition, the telomer chain may comprise a copolymeric mixture of uncharged and charged units. The distribution of the charges within the telomer, if present, may be random or blockwise.

In one preferrred embodiment of the invention, the telomer radical of formula (6a) is composed solely of non-ionic monomer units B and/or B'. In another preferred embodiment of the invention, the telomer radical of formula (6a) is composed solely of ionic monomer units B and/or B', for example solely of cationic monomer units or solely of anionic monomer units. Still another preferred embodiment of the invention is directed to telomer radicals of formula (6a) comprising nonionic units B and ionic units B'.

Suitable non-ionic substituents of B or B' include for example a radical C_1-C_6-alkyl which is substituted by one or more same or different substituents selected from the group consisting of -OH, C_1-C_4-alkoxy and -$NR_{23}R_{23}$', wherein R_{23} and R_{23}' are each independently of another hydrogen or unsubstituted or hydroxy-substituted C_1-C_6-alkyl or phenyl; phenyl which is substituted by hydroxy, C_1-C_4-alkoxy or -$NR_{23}R_{23}$', wherein R_{23} and R_{23}' are as defined above; a radical -COOY, wherein Y is C_1-C_{24}-alkyl which is unsubstituted or substituted, for example, by hydroxy, C_1-C_4-alkoxy, -O-Si$(CH_3)_3$, -$NR_{23}R_{23}$' wherein R_{23} and R_{23}' are as defined above, a radical -O-$(CH_2CH_2O)_{1\text{-}24}$-E wherein E is hydrogen or C_1-C_6-alkyl, or a radical -NH-C(O)-O-G, wherein -O-G is the radical of a saccharide with 1 to 8 sugar units or is a radical -O-$(CH_2CH_2O)_{1\text{-}24}$-E, wherein E is as defined above, or Y is C_5-C_8-cycloalkyl which is unsubstituted or substituted by C_1-C_4-alkyl or C_1-C_4-alkoxy, or is unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted phenyl or C_7-C_{12}-aralkyl; -$CONY_1Y_2$ wherein Y_1 and Y_2 are each independently hydrogen, C_1-C_{12}-alkyl, which is unsubstituted or substituted for example by hydroxy, C_1-C_4-alkoxy or a radical -O-$(CH_2CH_2O)_{1\text{-}24}$-E wherein E is as defined above, or Y_1 and Y_2 together with the adjacent N-atom form a five- or six-membered heterocyclic ring having no additional heteroatom or one additional oxygen or nitrogen atom; a radical -OY_3, wherein Y_3 is hydrogen; or C_1-C_{12}-alkyl which is unsubstituted or substituted by -$NR_{23}R_{23}$'; or is a radical -C(O)-C_1-C_4-alkyl; and wherein R_{23} and R_{23}' are as defined above; or a five- to seven-membered heterocyclic radical having at least one N-atom and being bound in each case via said nitrogen atom.

Suitable anionic substituents of B or B' include for example C_1-C_6-alkyl which is substituted by -SO_3H, -OSO_3H, -OPO_3H_2 and -COOH; phenyl which is substituted by one or more same or different substituents selected from the group consisting of -SO_3H, -COOH, -OH and -CH_2-SO_3H; -COOH; a radical -$COOY_4$, wherein Y_4 is C_1-C_{24}-alkyl which is substituted for example by -COOH, -SO_3H, -OSO_3H, -OPO_3H_2 or by a radical -NH-C(O)-O-G' wherein G' is the radical of an anionic carbohydrate; a radical -$CONY_5Y_6$ wherein Y_5 is C_1-C_{24}-alkyl which is substituted by -COOH, -SO_3H, -OSO_3H, or -OPO_3H_2 and Y_6 independently has the meaning of Y_5 or is hydrogen or C_1-C_{12}-alkyl; or -SO_3H; or a salt thereof, for example a sodium, potassium, ammonium or the like salt thereof.

Suitable cationic substituents of B or B' include C_1-C_{12}-alkyl which is substituted by a radical -$NR_{23}R_{23}'R_{23}''^+An^-$, wherein R_{23}, R_{23}' and R_{23}'' are each independently of another hydrogen or unsubstituted or hydroxy-substituted C_1-C_6-alkyl or phenyl, and An^- is an anion; or a radical -C(O)OY_7, wherein Y_7 is C_1-C_{24}-alkyl which is substituted by -$NR_{23}R_{23}'R_{23}''^+An^-$ and is further unsubstituted or substituted for example by hydroxy, wherein R_{23} R_{23}', R_{23}'' and An^- are as defined above.

Suitable zwitterionic substituents of B or B' include a radical -R_{24}-Zw, wherein R_{24} is a direct bond or a functional group, for example a carbonyl, carbonate, amide, ester, dicarboanhydride, dicarboimide, urea or urethane group; and Zw is an aliphatic moiety comprising one anionic and one cationic group each.

The following preferences apply to the hydrophilic substituents of B and B':
(i) non-ionic substituents:
Preferred alkyl substituents of B or B' are C_1-C_4-alkyl, in particular C_1-C_2-alkyl, which is substituted by one or more substituents selected from the group consisting of -OH and -$NR_{23}R_{23}'$, wherein R_{23} and R_{23}' are each independently of another hydrogen or C_1-C_4-alkyl, preferably hydrogen, methyl or ethyl and particularly preferably hydrogen or methyl, for example -CH_2-NH_2, -CH_2-$N(CH_3)_2$.
Preferred phenyl substituents of B or B' are phenyl which is substituted by -NH_2 or $N(C_1$-C_2-alkyl$)_2$, for example o-, m- or p-aminophenyl.
In case that the hydrophilic substituent of B or B' is a radical -COOY, Y as optionally substituted alkyl is preferably C_1-C_{12}-alkyl, more preferably C_1-C_6-alkyl, even more

preferably C_1-C_4-alkyl and particularly preferably C_1-C_2-alkyl, each of which being unsubstituted or substituted as mentioned above. In case that the alkyl radical Y is substituted by -$NR_{23}R_{23}$', the above-given meanings and preferences apply for R_{23} and R_{23}'. Examples of suitable saccharide substituents -O-G of the alkyl radical Y that is substituted by -NH-C(O)-O-G are the radical of a mono- or disaccharide, for example glucose, acetyl glucose, methyl glucose, glucosamine, N-acetyl glucosamine, glucono lactone, mannose, galactose, galactosamine, N-acetyl galactosamine, fructose, maltose, lactose, fucose, saccharose or trehalose, the radical of an anhydrosaccharide such as levoglucosan, the radical of a glucosid such as octylglucosid, the radical of a sugar alcohol such as sorbitol, the radical of a sugar acid derivative such as lactobionic acid amide, or the radical of an oligosaccharide with a maximum of 8 sugar units, for example fragments of a cyclodextrin, starch, chitosan, maltotriose or maltohexaose. The radical -O-G preferably denotes the radical of a mono- or disaccharide or the radical of a cyclodextrin fragment with a maximum of 8 sugar units. Particular preferred saccharide radicals -O-G are the radical of trehalose or the radical of a cyclodextrin fragment. In case that the alkyl radical Y is substituted by a radical -O-$(CH_2CH_2O)_{1-24}$-E or -NH-C(O)-O-G wherein -O-G is -O-$(CH_2CH_2O)_{1-24}$-E, the number of (CH_2CH_2O) units is preferably from 1 to 12 in each case and more preferably from 2 to 8. E is preferably hydrogen or C_1-C_2-alkyl.
Y as C_5-C_8-cycloalkyl is for example cyclopentyl or preferably cyclohexyl, each of which being unsubstituted or substituted for example by 1 to 3 C_1-C_2-alkyl groups.Y as C_7-C_{12}-aralkyl is for example benzyl.

Preferred nonionic radicals -COOY are those wherein Y is C_1-C_6-alkyl; or C_2-C_6-alkyl which is substituted by one or two substituents selected from the group consisting of hydroxy; ; C_1-C_2-alkoxy; -O-$Si(CH_3)_3$; and -$NR_{23}R_{23}$' wherein R_{23} and R_{23}' are each independently of another hydrogen or C_1-C_4-alkyl; or Y is a radical -CH_2CH_2-O-$(CH_2CH_2O)_{1-12}$-E wherein E is hydrogen or C_1-C_2-alkyl; or is a radical -C_2-C_4-alkylene-NH-C(O)-O-G, wherein -O-G is the radical of a saccharide.

More preferred non-ionic radicals -COOY are those wherein Y is C_1-C_4-alkyl; or C_2-C_4-alkyl which is substituted by one or two substituents selected from the group consisting of -OH and -$NR_{23}R_{23}$' wherein R_{23} and R_{23}' are each independently of another hydrogen or C_1-C_2-alkyl; or a radical -CH_2CH_2-O-$(CH_2CH_2O)_{1-12}$-E wherein E is hydrogen or C_1-C_2-alkyl; or is a radical -C_2-C_4-alkylene-NH-C(O)-O-G wherein -O-G is the radical of a saccharide.

Particularly preferred radicals -COOY comprise those wherein Y is C_1-C_2-alkyl, particularly methyl; or C_2-C_3-alkyl, which is unsubstituted or substituted by hydroxy or N,N-di-C_1-C_2-alkylamino, or is a radical -C_2-C_3-alkylene-NH-C(O)-O-G wherein -O-G is the radical of trehalose or the radical of a cyclodextrin fragment with a maximum of 8 sugar units.

Preferred non-ionic substituents -C(O)-NY_1Y_2 of B or B' are those wherein Y_1 and Y_2 are each independently of the other hydrogen or C_1-C_6-alkyl which is unsubstituted or substituted by hydroxy; or Y_1 and Y_2 together with the adjacent N-atom form a heterocyclic 6-membered ring having no further heteroatom or having one further N- or O-atom. Even more preferred meanings of Y_1 and Y_2, independently of each other, are hydrogen or C_1-C_4-alkyl which is unsubstituted or substituted by hydroxy; or Y_1 and Y_2 together with the adjacent N-atom form a N-C_1-C_2-alkylpiperazino or morpholino ring. Particularly preferred non-ionic radicals -C(O)-NY_1Y_2 are those wherein Y_1 and Y_2 are each independently of the other hydrogen or C_1-C_2-alkyl; or Y_1 and Y_2 together with the adjacent N-atom form a morpholino ring.

Preferred non-ionic substituents -OY_3 of B or B' are those wherein Y_3 is hydrogen, C_1-C_4-alkyl which is unsubstituted or substituted by -NH_2 or -N(C_1-C_2-alkyl)$_2$, or is a group -C(O)C_1-C_2-alkyl. Y_3 is particularly preferred hydrogen or acetyl.

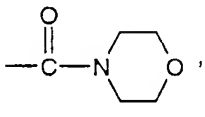
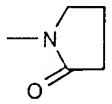
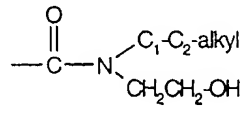
Preferred non-ionic heterocyclic substituents of B or B' are a 5- or 6-membered heteroaromatic or heteroaliphatic radical having one N-atom and in addition no further heteroatom or an additional N- or O- heteroatom, or is a 5 to 7-membered lactame. Examples of such heterocyclic radicals are N-pyrrolidonyl, 2- or 4-pyridinyl, 2-methyl pyridin-5-yl, 2-, 3- oder 4-hydroxypyridinyl, N-ε-caprolactamyl, N-imidazolyl, 2-methylimidazol-1-yl, N-morpholinyl or 4-N-methylpiperazin-1-yl, particularly N-morpholinyl or N-pyrrolidonyl.

A group of preferred non-ionic substituents of B or B' comprises C_1-C_2-alkyl, which is unsubstituted or substituted by -OH or -$NR_{23}R_{23}'$, wherein R_{23} and R_{23}' are each independently of the other hydrogen or C_1-C_2-alkyl; a radical -COOY wherein Y is C_1-C_4-alkyl; C_2-C_4-alkyl which is substituted by -OH, -$NR_{23}R_{23}'$ wherein R_{23} and R_{23}' are each independently of another hydrogen or C_1-C_2-alkyl, or Y is a radical -C_2-C_4-alkylene-NH-C(O)-O-G wherein -O-G is the radical of a saccharide; a radical -C(O)-NY_1Y_2, wherein Y_1 and Y_2

are each independently of the other hydrogen or C_1-C_6-alkyl which is unsubstituted or substituted by hydroxy, or Y_1 and Y_2 together with the adjacent N-atom form a heterocyclic 6-membered ring having no further heteroatom or having one further N- or O-atom; a radical $-OY_3$, wherein Y_3 is hydrogen, C_1-C_4-alkyl which is unsubstituted or substituted by $-NH_2$ or $-N(C_1$-C_2-alkyl$)_2$, or is a group $-C(O)C_1$-C_2-alkyl; or a 5- or 6-membered heteroaromatic or heteroaliphatic radical having one N-atom and in addition no further heteroatom or an additional N-, O- or S-heteroatom, or a 5 to 7-membered lactame.

A group of more preferred non-ionic substituents of B or B' comprises a radical -COOY, wherein Y is C_1-C_2-alkyl, C_2-C_3-alkyl, which is substituted by hydroxy, amino or N,N-di-C_1-C_2-alkylamino, or is a radical $-C_2$-C_4-alkylene-NH-C(O)-O-G wherein -O-G is the radical of trehalose; a radical $-CO-NY_1Y_2$, wherein Y_1 and Y_2 are each independently of the other hydrogen or C_1-C_4-alkyl which is unsubstituted or substituted by hydroxy, or Y_1 and Y_2 together with the adjacent N-atom form a N-C_1-C_2-alkylpiperazino or morpholino ring; or a heterocyclic radical selected from the group consisting of N-pyrrolidonyl, 2- or 4-pyridinyl, 2-methylpyridin-5-yl, 2-, 3- oder 4-hydroxypyridinyl, N-ε-caprolactamyl, N-imidazolyl, 2-methylimidazol-1-yl, N-morpholinyl and 4-N-methylpiperazin-1-yl.

A particularly preferred group of non-ionic substituents of B or B' comprises the radicals

$-CONH_2$, $-CON(CH_3)_2$,  ,  ,  ,

$-CONH-(CH_2)_2-OH$, $-COO-(CH_2)_2-N(CH_3)_2$, and $-COO(CH_2)_{2\text{-}4}-NHC(O)-O-G$ wherein -O-G is the radical of trehalose.

(ii) anionic substituents:

Preferred anionic substituents of B or B' are C_1-C_4-alkyl, in particular C_1-C_2-alkyl, which is substituted by one or more substituents selected from the group consisting of $-SO_3H$ and $-OPO_3H_2$, for example $-CH_2-SO_3H$; phenyl which is substituted by $-SO_3H$ or sulfomethyl, for example o-, m- or p-sulfophenyl or o-, m- or p-sulfomethylphenyl; -COOH; a radical $-COOY_4$, wherein Y_4 is C_2-C_6-alkyl which is substituted by -COOH, $-SO_3H$, $-OSO_3H$, $-OPO_3H_2$, or by a radical -NH-C(O)-O-G' wherein G' is the radical of lactobionic acid, hyaluronic acid or sialic acid, in particular C_2-C_4-alkyl which is substituted by $-SO_3H$ or -

OSO_3H; a radical $-CONY_5Y_6$ wherein Y_5 is C_1-C_6-alkyl substituted by sulfo, in particular C_2-C_4-alkyl substituted by sulfo, and Y_6 is hydrogen, for example the radical $-C(O)-NH-C(CH_3)_2-CH_2-SO_3H$; or $-SO_3H$; or a suitable salt thereof. Particular preferred anionic substituents of B or B' are -COOH, $-SO_3H$, o-, m- or p-sulfophenyl, o-, m- or p-sulfomethylphenyl or a radical $-CONY_5Y_6$ wherein Y_5 is C_2-C_4-alkyl substituted by sulfo, and Y_6 is hydrogen.

(iii) cationic substituents:

Preferred cationic substituents of B or B' are C_1-C_4-alkyl, in particular C_1-C_2-alkyl, which is in each case substituted by $-NR_{23}R_{23}'R_{23}''^{+}An^-$; or a radical $-C(O)OY_7$ wherein Y_7 is C_2-C_6-alkyl, in particular C_2-C_4-alkyl, which is in each case substituted by $-NR_{23}R_{23}'R_{23}''^{+}An^-$ and is further unsubstituted or substituted by hydroxy. R_{23}, R_{23}' and R_{23}'' are each independently of another preferably hydrogen or C_1-C_4-alkyl, more preferably methyl or ethyl and particularly preferably methyl. Examples of suitable anions An^- are Hal^-, wherein Hal is halogen, for example Br^-, F^-, J^- or particularly Cl^-, furthermore HCO_3^-, CO_3^{2-}, $H_2PO_3^-$, HPO_3^{2-}, PO_3^{3-}, HSO_4^-, SO_4^{2-} or the radical of an organic acid such as $OCOCH_3^-$ and the like. A particularly preferred cationic substituent of B or B' is a radical $-C(O)OY_7$ wherein Y_7 is C_2-C_4-alkyl, which is substituted by $-N(C_1\text{-}C_2\text{-alkyl})_3^+An^-$ and is further substituted by hydroxy, and An^- is an anion, for example the radical $-C(O)O-CH_2-CH(OH)-CH_2-N(CH_3)_3^+An^-$.

(iv) zwitterionic substituents $-R_{24}$-Zw:

R_{24} is a preferably a carbonyl, ester or amide functional group and more preferably an ester group -C(O)-O-.

Suitable anionic groups of the moiety Zw are for example $-COO^-$, $-SO_3^-$, $-OSO_3^-$, $-OPO_3H^-$ or bivalent $-O-PO_2^-$- or $-O-PO_2^--O-$, preferably a group $-COO^-$ or $-SO_3^-$ or a bivalent group $-O-PO_2^-$-, and in particular a group $-SO_3^-$.

Suitable cationic groups of the moiety Zw are for example a group $-NR_{23}R_{23}'R_{23}''^{+}$ or a bivalent group $-NR_{23}R_{23}'^{+}$-, wherein R_{23}, R_{23}' and R_{23}'' are as defined above, and are each independently of the other, preferably hydrogen or C_1-C_6-alkyl, preferably hydrogen or C_1-C_4-alkyl and most preferably each methyl or ethyl.

The moiety Zw is for example C_2-C_{30}-alkyl, preferably C_2-C_{12}-alkyl, and more preferably C_3-C_8-alkyl, which is in each case uninterrupted or interrupted by -O- and substituted or interrupted by one of the above-mentioned anionic and cationic groups each, and, in

addition, is further unsubstituted or substituted by a radical $-OY_8$, wherein Y_8 is hydrogen or the acyl radical of a carboxylic acid.

Y_8 is preferably hydrogen or the acyl radical of a higher fatty acid.

Zw is preferably C_2-C_{12}-alkyl and even more preferably C_3-C_8-alkyl which is substituted or interrupted by one of the above-mentioned anionic and cationic groups each, and in addition may be further substituted by a radical $-OY_8$.

A preferred group of zwitter-ionic substituents $-R_{24}$-Zw corresponds to the formula

$$-C(O)O-(alk''')-N(R_{23})_2^+-(alk')-An^- \quad \text{or}$$

$$-C(O)O-(alk'')-O-PO_2^--(O)_{0-1}-(alk''')-N(R_{23})_3^+$$

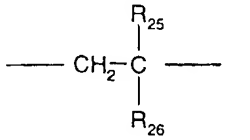
wherein R_{23} is hydrogen or C_1-C_6-alkyl; An^- is an anionic group $-COO^-$, $-SO_3^-$, $-OSO_3^-$ or $-OPO_3H^-$, preferably $-COO^-$ or $-SO_3^-$ and most preferably $-SO_3^-$, alk' is C_1-C_{12}-alkylene, (alk'') is C_2-C_{24}-alkylene which is unsubstituted or substituted by a radical $-OY_8$, Y_8 is hydrogen or the acyl radical of a carboxylic acid, and (alk''') is C_2-C_8-alkylene.

(alk') is preferably C_2-C_8-alkylene, more preferably C_2-C_6-alkylene and most preferably C_2-C_4-alkylene. (alk'') is preferably C_2-C_{12}-alkylene, more preferably C_2-C_6-alkylene and particularly preferably C_2-C_3-alkylene which is in each case unsubstituted or substituted by hydroxy or by a radical $-OY_8$. (alk''') is preferably C_2-C_4-alkylene and more preferably C_2-C_3-alkylene. R_{23} is hydrogen or C_1-C_4-alkyl, more preferably methyl or ethyl and particularly preferably methyl. A preferred zwitterionic substituent of B or B' is of formula

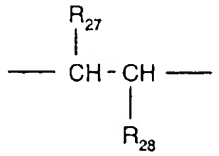
$$-C(O)O-CH_2-CH(OY_8)-CH_2-O-PO_2^--(CH_2)_2-N(CH_3)_3^+,$$

wherein Y_8 is hydrogen or the acyl radical of a higher fatty acid.

B denotes for example a radical of formula



(7a) or



(7b),

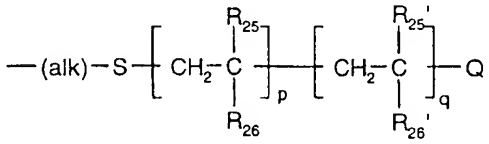
wherein R_{25} is hydrogen or C_1-C_4-alkyl, preferably hydrogen or methyl; R_{26} is a hydrophilic substituent, wherein the above given meanings and preferences apply; R_{27} is C_1-C_4-alkyl, phenyl or a radical $-C(O)OY_9$, wherein Y_9 is hydrogen or unsubstituted or hydroxy-

substituted C_1-C_4-alkyl; and R_{28} is a radical -C(O)Y_9' or -CH_2-C(O)OY_9' wherein Y_9' independently has the meaning of Y_9.

R_{27} is preferably C_1-C_2-alkyl, phenyl or a group -C(O)OY_9. R_{28} is preferably a group -C(O)OY_9' or -CH_2-C(O)OY_9' wherein Y_9 and Y_9' are each independently of the other hydrogen, C_1-C_2-alkyl or hydroxy-C_1-C_2-alkyl. Particularly preferred -CHR_{27}-CHR_{28}- units according to the invention are those wherein R_{27} is methyl or a group -C(O)OY_9 and R_{28} is a group -C(O)OY_9' or -CH_2-C(O)OY_9' wherein Y_9 and Y_9' are each hydrogen, C_1-C_2-alkyl or hydroxy-C_1-C_2-alkyl.

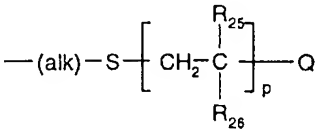
B' independently may have one of the meanings given above for B.

If (oligomer) is a radical of formula (6a), the radical -(alk)-S-$[B]_p$-$[B']_q$-Q preferably denotes a radical of formula



(6a') and

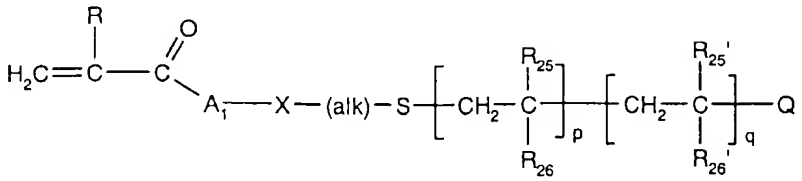
even more preferably of the formula



(6a''),

wherein for R_{25}, R_{26}, Q, p and q the above-given meanings and preferences apply, for R_{25}' independently the meanings and preferences given before for R_{25} apply, and for R_{26}' independently the meanings and preferences given before for R_{26} apply.

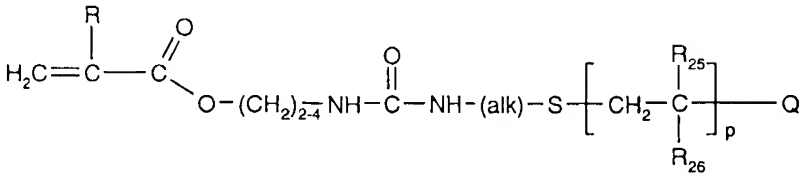
A preferred group of suitable hydrophilic macromonomers according to step (c) of the invention comprises compounds of formula



(4a),

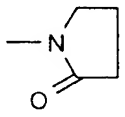
wherein R is hydrogen or methyl, A_1 is -O-$(CH_2)_{2-4}$-, -O-CH_2-CH(OH)-CH_2- or a radical -O-$(CH_2)_{2-4}$-NH-C(O)-, X is -O- or -NH-, (alk) is C_2-C_4-alkylene, Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, p is an integer from 5 to 50, R_{25} and R_{25}' are each independently of the other hydrogen or methyl, and for R_{26} and R_{26}' each independently the above given meanings and preferences apply.

A particularly preferred embodiment of the invention relates to hydrophilic macromonomers of the formula



(4b),

wherein for R, R_{25}, R_{26}, Q, (alk) and p the above-given meanings and preferences apply. A particularly preferred group of hydrophilic macromonomers are compounds of the above formula (4b) wherein R is hydrogen or methyl, (alk) is C_2-C_4-alkylene, R_{25} is hydrogen or methyl, p is an integer of 5 to 50, Q is as defined before, and for R_{26} the above given meanings and preferences apply; in particular R_{26} of this embodiment is a radical

-$CONH_2$, -$CON(CH_3)_2$ or  .

If (oligomer) is a radical (ii) of formula (6b), Q' in formula (6b) is for example C_1-C_{12}-alkyl, phenyl or benzyl, preferably C_1-C_2-alkyl or benzyl and in particular methyl. R_{19} is preferably unsubstituted or hydroxy-substituted C_1-C_4-alkyl and in particular methyl. u is preferably an integer from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50.

If (oligomer) is a radical of formula (6b'), the above given meanings and preferences apply for the variables R_{19} and u contained therein. X in formula (6b') is preferably hydroxy or amino.

If (oligomer) denotes a radical (iv) of formula (6c), R_{20} and R_{20}' are each preferably ethyl or in particular methyl; v is preferably an integer from 2 to 150, more preferably from 5 to 100,

even more preferably from 5 to 75 and particularly preferably from 10 to 50; Q" is for example hydrogen; and An^- is as defined before.

If (oligomer) denotes an oligopeptide radical (v) of formula (6d) or 6d'), R_{21} is for example hydrogen, methyl, hydroxymethyl, carboxymethyl, 1-hydroxyethyl, 2-carboxyethyl, isopropyl, n-, sec. or iso-butyl, 4-amino-n-butyl, benzyl, p-hydroxybenzyl, imidazolylmethyl, indolylmethyl or a radical $-(CH_2)_3-NH-C(=NH)-NH_2$. t is preferably an integer from 2 to 150, more preferably from 5 to 100, even more preferably from 5 to 75 and particularly preferably from 10 to 50.

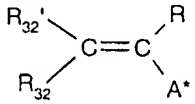
If (oligomer) denotes a polyoxyalkylene radical (vi) of formula (6e), R_{34} is preferably hydrogen or C_1-C_{18}-alkyl, more preferably hydrogen or C_1-C_{12}-alkyl, even more preferably hydrogen, methyl or ethyl, and particularly preferably hydrogen or methyl. ($alk^{"}$) is preferably a C_2-C_3-alkylene radical. z is preferably 0. r and s are each independently preferably an integer from 0 to 100 wherein the total of (r+s) is 5 to 100. r and s are each independently more preferably an integer from 0 to 50 wherein the total of (r+s) is 8 to 50. In a particularly preferred embodiment of the polyoxyalkylene radicals (oligomer), r is an integer from 8 to 50 and particularly 9 to 25, and s is 0.

(oligomer) as the radical of an oligosaccharide (vii) may be, for example, a di- or polysaccharide including carbohydrate containing fragments from a biopolymer. Examples are the radical of a cyclodextrin, trehalose, cellobiose, maltotriose, maltohexaose, chitohexaose or a starch, hyaluronic acid, deacetylated hyaluronic acid, chitosan, agarose, chitin 50, amylose, glucan, heparin, xylan, pectin, galactan, glycosaminoglycan, mucin, dextran, aminated dextran, cellulose, hydroxyalkylcellulose or carboxyalkylcellulose oligomer, each of which with a molecular weight average weight of, for example, up to 25000, preferably up to 10000. Preferably the oligosaccharide according to (vii) is the radical of a cyclodextrin with a maximum of 8 sugar units.

Formulae (6a), (6a') or (6e) are to be understood as a statistic description of the respective oligomeric radicals, that is to say, the orientation of the monomers and the sequence of the monomers (in case of copolymers) are not fixed in any way by said formulae. The arrangement of B and B' in formula (6a) or of the ethyleneoxide and propyleneoxide units in formula (6e) thus in each case may be random or blockwise.

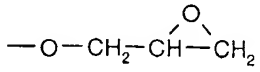
The weight average molecular weight of the hydrophilic macromonomer according to step (c) depends principally on the desired properties and is for example from 300 to 25000, preferably from 300 to 12000, more preferably from 300 to 8000, even more preferably from 300 to 5000, and particularly preferably from 500 to 4000.

The macromonomers of formula (4) may be prepared by methods known per se. For example, the compounds of formula (4) wherein A is a radical of formula (5a), (5b) or (5d) are obtainable by reacting a compound of formula



(8)

wherein R, R_{32} and R_{32}' each have the above-given meaning and A* is, for example, a group -C(O)-A**, wherein A** is halogen, particularly chlorine, an ester group an oxyalkylene radical comprising an epoxy group, for example the radical

 ; or is a radical -O-C_2-C_{12}-alkylene-N=C=O; or A* is a radical

-$(A_2)_m$-N=C=O, wherein A_2 and m have the above-given meaning, with a compound of formula

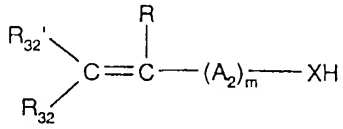
HX - (oligomer) (9),

wherein X has the above-given meaning.

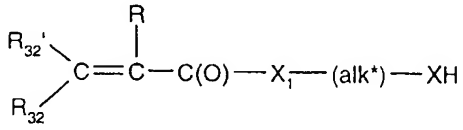
The reactions of a compound of formula (8) having a carboxylic acid halide group, an epoxy group or an isocyanato group with an amino or hydroxy compound of formula (9) are well-known in the art and may be carried out as desribed in textbooks of organic chemistry. For example, the reaction of an isocyanato derivative of formula (8) with a compound of formula (9) may be carried out in an inert organic solvent such as an optionally halogenated hydrocarbon, for example petroleum ether, methylcyclohexane, toluene, chloroform, methylene chloride and the like, or an ether, for example diethyl ether, tetrahydrofurane, dioxane, or a more polar solvent such as DMSO, DMA, N-methylpyrrolidone or even a lower alcohol, at a temperature of from 0 to 100°C, preferably from 0 to 50°C and particularly preferably at room temperature, optionally in the presence of a catalyst, for example a tertiary amine such as triethylamine or tri-n-butylamine, 1,4-diazabicyclooctane, or a tin

compound such as dibutyltin dilaurate or tin dioctanoate. In addition, the reaction of an isocyanato derivative of formula (8) with a compound of formula (9) wherein -XH is an amino group also may be carried out in an aqueous solution in the absence of a catalyst. It is advantageous to carry out the above reactions under an inert atmosphere, for example under an nitrogen or argon atmosphere.

Moreover, the macromonomers of formula (4) wherein A is a radical of formula (5c) or (5e) may be obtained by reacting a compound of formula



(10a) or



(10b),

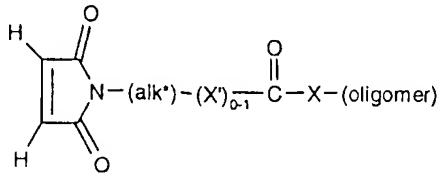
wherein R, R_{32}, R_{32}', A_2, X, X_1, (alk*) and m each have the above-given meaning, with a compound of formula

$$-X_1'(O)C - (\text{oligomer}) \qquad (9a),$$

wherein (oligomer) has the above-given meaning and X_1' is for example -OH or halogen, in particular chlorine, or together with -(O)C- forms an anhydride group, in a manner known per se.

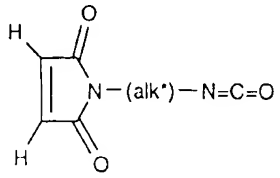
The macromonomers of formula (4), wherein A is a direct bond and (oligomer) is a radical of formula (6c') are known or may be prepared according to methods known in the art, for example as described in S. Kobayashi et al., Polymer Bulletin 13, p 447-451 (1985).

Likewise, the macromonomers of the formula



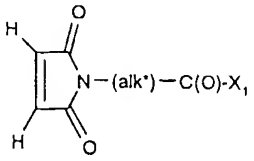
(4c),

wherein (alk*), X', X and (oligomer) each have the above-given meaning, may be obtained in a manner known per se, for example, by reacting a compound of formula



(12),

wherein (alk*) has the above-given meaning, with a compound of the above-given formula (6), or by reacting a compound of formula



(12a)

with a compound of the above formula (9) wherein (alk*) and X_1 each have the above-given meaning.

The compounds of the formula (8), (9), (9a), (10a), (10b), (12) and (12a) are known compounds which are commercially available or may be prepared according to known methods. For example, compounds of the formula (9) and (9a) wherein (oligomer) denotes a radical of formula (6a) may be prepared according to PCT application WO 92/09639 by copolymerizing one or more hydrophilic ethylenically unsaturated monomers in the presence of a functional chain transfer agent such as cysteamine hydrochloride, thioglycolic acid or the like.

The hydrophilic monomers or macromonomers may be applied to the initiator-modified material and polymerized there according to processes known per se. For example, the material comprising the covalently bound polymerisation initiator is immersed in a solution of the monomer or macromonomer, or a layer of monomer or macromonomer is first of all deposited on the modified material surface, for example, by dipping, spraying, spreading, knife coating, pouring, rolling, spin coating or vacuum vapor deposition. Suitable solvents, if used in the polymerization process, are, for example, water or dipolar aprotic solvents such as, for example, acetonitrile. The polymerization of the hydrophilic monomer or macromonomer on the material comprising the primary polymer coating then may be initiated , for example, thermally by the action of heat or preferably by irradiation, particularly by UV radiation. Suitable light sources for the irradiation are known to the artisan and comprise for example mercury lamps, high pressure mercury lamps, xenon lamps, carbon

arc lamps or sunlight. The time period of irradiation may depend for example on the desired properties of the resulting composite material but is usually in the range of up to 30 minutes, preferably from 10 secondes to 10 minutes, and particularly preferably from 0.5 to 5 minutes. It is advantageous to carry out the irradiation in an atmosphere of inert gas. After the polymerization, any non-covalently bound monomers, polymers, oligomers or non-reacted macromonomers formed can be removed, for example by treatment with suitable solvents.

The coated material obtained according to the invention may be purified afterwards in a manner known per se, for example by washing or extraction with a suitable solvent such as water.

By means of process step (c) of the above-described coating process, the hydrophilic macromonomers may be grafted to the material surface with formation of a coating having, for example, a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains. Such BBT structures in one embodiment comprise a long hydrophilic or hydrophobic backbone which carries relatively densely packed comparatively short hydrophilic side chains (called primary bottle brushes). Another embodiment relates to secondary bottle brushes which are characterized in that the hydrophilic side chains themselves carry densely packed hydrophilic "secondary" side chains. Polymeric coatings of said primary and secondary BBT structures to a certain extent mimic highly water-retaining structures occurring in the human body, for example in cartilage or mucosal tissue.

The coating thickness of the macromonomers depends principally on the desired properties. It can be, for example, from 0.001 to 1000 µm, preferably from 0.005 to 100 µm, more preferably from 0.01 to 50 µm, even more preferably from 0.01 to 5 µm, especially preferably from 0.01 to 1 µm and particularly preferably from 0.01 to 0.5 µm.

A further embodiment of the invention relates to a material that is coated by the process of the invention.

The material that is coated by the process of the invention is, for example, an organic bulk material, preferably a biomedical device, e.g. an ophthalmic device, preferably a contact

lens including both hard and particularly soft contact lenses, an intraocular lens or artificial cornea. Further examples are materials useful for example as wound healing dressings, eye bandages, materials for the sustained release of an active compound such as a drug delivery patch, moldings that can be used in surgery, such as heart valves, vascular grafts, catheters, artificial organs, encapsulated biologic implants, e.g. pancreatic islets, materials for prostheses such as bone substitutes, or moldings for diagnostics, membranes or biomedical instruments or apparatus.

The biomedical devices, e.g. ophthalmic devices obtained according to the invention have a variety of unexpected advantages over those of the prior art which make those devices very suitable for practical purposes,e.g. as contact lens for extended wear or intraocular lens. For example, they do have a high surface wettability which can be demonstrated by their contact angles, their water retention and their water-film break up time or tear film break up time (TBUT).

The TBUT plays an particularly important role in the field of ophthalmic devices such as contact lenses. Thus the facile movement of an eyelid over a contact lens has proven important for the comfort of the wearer; this sliding motion is fa cilitated by the presence of a continuous layer of tear fluid on the contact lens, a layer which lubricates the tissue/lens interface. However, clinical tests have shown that currently available contact lenses partially dry out between blinks, thus increasing friction between eyelid and the lens. The increased friction results in soreness of the eyes and reduced movement of the contact lenses. Now it has become feasible to considerably increase the TBUT of commercial contact lenses such as, for example, those made of nelfilcon A, vifilcon A or lotrafilcon A polymer, by applying a surface coating according to the invention. On the base curve of a contact lens, the pronounced lubricity of the coating facilitates the on-eye lens movement which is essential for extended wear of contact lenses. Moreover, the materials obtained by the process of the invention provide additional effects being essential for lenses for extended wear, such as an increased thickness of the pre-lens tear film which contributes substantially to low microbial adhesion and resistance to deposit formation. Due to the extremely soft and lubricious character of the novel surface coatings, biomedical articles such as in particular contact lenses coated by the process of the invention show a superior wearing comfort including improvements with respect to late day dryness and long term (overnight) wear. The novel

surface coatings moreover interact in a reversible manner with occular mucus which contributes to the improved wearing comfort.

In addition, biomedical devices, e.g. ophthalmic devices such as contact lenses, coated by the process of the invention, have a very pronounced biocompatibility combined with good mechanical properties. For example, the devices are blood compatible and have a good tissue integration. In addition, there are generally no adverse eye effects observed, while the adsorption of proteins or lipids is low, also the salt deposit formation is lower than with conventional contact lenses. Generally, there is low fouling, low microbial adhesion and low bioerosion while good mechanical properties can be for example found in a low friction coefficient and low abrasion properties. Moreover, the dimensional stability of the materials obtained according to the invention is excellent. In addition, the attachment of a hydrophilic surface coating at a given bulk material according to the invention does not affect its visual transparency.

In summary, the ophthalmic devices obtained by the process of the invention, such as contact lenses and artificial cornea, provide a combination of low spoilation with respect to cell debris, cosmetics, dust or dirt, solvent vapors or chemicals, with a high comfort for the patient wearing such opthalmic devices in view of the soft hydrogel surface which for example provides a very good on-eye movement of the ohthalmic device.

Biomedical devices such as renal dialysis membranes, blood storage bags, pacemaker leads or vascular grafts coated by the process of the invention resist fouling by proteins by virtue of the continuous layer of bound water, thus reducing the rate and extent of thrombosis. Blood-contacting devices fabricated according to the present invention are therefore haemocompatible and biocompatible.

In the examples, if not indicated otherwise, amounts are amounts by weight, temperatures are given in degrees Celsius. Tear break-up time values in general relate to the pre-lens tear film non-invasive break-up time (PLTF-NIBUT) that is determined following the procedure published by M. Guillon et al., Ophthal. Physiol. Opt. 9, 355-359 (1989) or M. Guillon et al., Optometry and Vision Science 74, 273-279 (1997). Average advancing and receding water contact angles of coated and non-coated lenses are determined with the dynamic Wilhelmy method using a Krüss K-12 instrument (Krüss GmbH, Hamburg, Germany). Wetting force on

the solid is measured as the solid is immersed in or withdrawn from a liquid of known surface tension.

Examples A1-A4: Spray coating on contact lenses using azido aniline hydrochloride

A solution of 0.1 mg/ml azido aniline hydrochloride in methanol is given into a funnel of an airbrush (aero-pro 381™, Hansa). The solution is sprayed onto both sides of wet or dried lotrafilcon A lenses (polysiloxane/perfluoroalkylpolyether copolymer) for the time as indicated in the Table below using a nitrogen pressure of 1.15 bar. Afterwards the lenses are irradiated 30 seconds using a UV lamp (LQ 400B, Gröbel) with an intensity of 1.43 mW/cm^2 and a 305 nm cutoff filter. The whole process is optionally repeated. The lenses are then extracted in acetonitrile/methanol 80/20 overnight.

Table

Example	Spray time in seconds/ number of spray cycles	Lens surfaces before spraying
A-1	3/1	dry
A-2	7/1	dry
A-3	7/1	wet
A-4	7/3	dry

Example A-5: Surface Functionalization of contact lenses using a benzophenone

Uncoated lotrafilcon A silicone-hydrogel contact lenses are placed in a 3 cm Petri dish and treated with 10 ml of a 2 % w/w solution of benzophenone-3,4,3',4'-tetracarboxylic acid dianhydride (BTDA) in formamide by gentle shaking for 6 minutes. The Petri dish is then exposed to UV irradiation for 2 minutes under ambient conditions using a Groebel RM-3 lamp. Excessive BTDA is removed from the lens surfaces by repeated rinses with formamide and water.

Example A-6: Surface Functionalization of contact lenses using a benzophenone

A drop of the BTDA solution as prepared in Example A-5 is placed in the female part of a polypropylene (PP) contact lens mold. A lotrafilcon A contact lens is then placed into that mold on a way that the BTDA solution forms a thin capillary layer between mold surface and

lens surface. A second drop of the BTDA solution is placed in the cavity of the lens and the PP mold is finally closed by putting it's male part on top. The mold is only weakly clamped in order to maintain capillary layers of BTDA solution on both sides of the contact lens. The molds are then simultaneously UV irradiated from both sides for 60 seconds. After removal from the molds the contact lenses thus treated are rinsed with formamide and water and finally autoclaved in water fo 30 minutes at 121 °C.

Example A-7: Surface Funtionalization of contact lenses using a benzophenone

As described in Examples A-5 and A-6 lotrafilcon A contact lenses are treated with a BTDA solution in formamide which contains in addition 0,2 % of the surfactant Silwet L77 (Wacker, Burghausen/Germany). The lenses are dipped 3-times for 30 seconds in the solution, placed onto a polypropylene film, then UV irradiated for 2 minutes and rinsed.

Example A-8: Surface Functionalization of contact lenses using a benzophenone

Lotrafilcon A contact lenses are sprayed on both sides with a 10 % w/w solution of benzophenone-tetracarboxylic acid sodium salt (BTA-Na) in water, using a commercially available paint brush. The lenses are then UV irradiated for 1 minute, rinsed 3-times in water and autoclaved in water at 121 °C for 30 minutes. The uniformity of the surface functionalization, the polarity of the lens surfaces as well as their overall functionality can be improved by applying repeated spray/UV-irradiation cycles to the lenses.

Example A-9: Surface functionalization of contact lenses using a benzophenone

According to the method described in Example A-8 lotrafilcon A contact lenses were spray-/UV- treated in repeated cycles using a 10 % w/w solution of BTDA in THF, methylethylketone (MEK) or dimethylacetamide (DMAc).

Examples A-10 – A-13: Quantification of BTDA surface groups on contact lenses by spin-labelling and ESR-Spectroscopy

Anhydride functionalized lenses are prepared as described in examples A-5 – A-9 (without autoclaving) and then treated at 25 °C for 10 hours with a 1 % w/w solution of the spin label 4-amino-2,2,6,6-tetramethyl-piperidine-N-oxide (4-amino-TEMPO) in acetonitrile. After careful extraction of only physically adsorbed excessive spin label molecules the lenses are

investigated by ESR-spectroscopy. The concentration of functional anhydride groups on the lens surfaces is extrapolated from the total number of mmoles of bound nitroxyl radicals per lens.

Example No.	Funtionalized lenses from Example No.	Concentration of anhydride groups [anhydride groups / nm^2]
A-10	A-5	26,3
A-11	A-6	13,2
A-12	A-7	5,8
A-13	A-9	7,3

Examples A-14 – A-15: Surface functionalization of contact lenses using 3,3'-Diamino-benzophenone (3,3'-DAB) and 3,4-Diamino-benzophenone (3,4-DAB)

As outlined in Examples A-8 and A-9 lotrafilcon A contact lenses are functionalized by spray-treament/UV-irradiation with 5 % w/w aqueous solutions of the 3,3'-DAB hydrochloride (A-14) or 3,4-DAB hydrochloride (A-15) using in each case 4 repeated cycles of spraying and UV irradiation. After careful rinsing with water the lenses are treated at 25 °C for 30 minutes with a 10 % w/w solution of triethylamine in acetonitrile.

Examples B1 – B-4: Surface binding of reactive photoinitiator molecules

The aminofunctionalized contact lenses from Examples A-1 – A-4 are immersed into a 1% by weight solution of the reactive photoinitiator prepared by the addition reaction from isophorone diisocyanate and 4-(2-hydroxyethoxy)phenyl 2-hydroxy-2-propyl ketone (Darocure 2959) (synthesis see EP 0 632 329) in acetonitrile. 3 drops of triethylamine (TEA) are then added to the solution. The amino groups on the lens surface react with the isocyanato groups of the photoinitiator molecules for 12 hours. After this time, the lenses are withdrawn from the reaction solution, 3x washed and extracted in acetonitrile for 8 hours and dried under reduced pressure for 2 hours. The dried lenses are subsequently used for photografting.

Example B-5 - B-8: Surface binding of the reactive photoinitiator molecules

The aminofunctionalized contact lenses from Examples A-1 to A-4 are dried to the constant mass under reduced pressure. The lenses are then directly immersed into 1% by weight

acetonitrile solution of the reactive photoinitiator prepared by the addition reaction from isophorone diisocyanate and 2-dimethylamino-2-benzyl-1-[4-(2-hydroxyethoxy)phenyl]-butan-1-one (synthesis see WO 96/20796 (5 ml solution/lens). 3 drops of triethylamine (TEA) are then added to the solution. The amino groups on the lens surface react with the isocyanato groups of the photoinitiator molecules for 12 hours. After this time, the lenses are withdrawn from the reaction solution, 3x washed and extracted in acetonitrile for 6 hours and dried under reduced pressure for 2 hours. The dried lenses are subsequently used for photografting.

Example B-9: Surface binding of the reactive photoinitiator molecules

Using the method outlined in Example B-1 surface funtionalized lotrafilcon A contact lenses prepared in Example A-15 are treated with a 1% w/w acetonitrile solution of the reactive photoinitiator. The dried lenses are subsequently used for photografting.

Example C-1: Acrylamide telomer (M_n 2000 Da) synthesis

A 1000 ml round bottom flask is charged with a solution of 71.1g (1 mol) acrylamide, 4.93g (18.2 mmol) α,α'-azodiisobutyramidine dihydrochloride and 4.93 g (36.4 mmol) cysteamin-hydrochloride in 400 ml of water. The clear and slightly yellowish solution is acidified with a few drops of hydrochloric acid to pH3. The stirred acidic solution is evacuated to 50 mbar and filled with argon. This is repeated three times. With a constant stream of Argon, this solution is poured into a 500 ml dropping funnel which is put onto an 'flow-through-reactor' consisting of an 1000ml three-necked round-bottom flask, reflux condenser, thermometer, magnetic stirrer and a 30 cm Liebig-condenser, which is filled with glass wool. The whole apparatus is constantly purged with argon. The dropping funnel is put onto the Liebig condenser, which is heated to 65°C. The flask is heated to 60°C. The solution is slowly dropped through the Liebig–condenser into the stirred flask. This takes 2.5 hrs. During this time the temperature in the flask is kept between 58-65°C. After the completed addition, the solution is stirred for 2hrs at 60°C.

NaOH is added to the clear and slightly yellowish solution until pH 10 is reached. The product is purified through reverse osmosis, using Millipore cartridge with a cut-off at 1000 Da and freeze-dried. A bright-white solid product is obtained (NH_2 0.34mEq/g ,sulfur-value of the elemental analysis (0.33mEq/g); M_n 2000 Da).

Example C-2: Acrylamide telomer (M_n 1350 Da) synthesis

A 1000 mL round bottom flask is charged with a solution of 99.5 g (1.46 mol) acrylamide, 1.27 g (4.68 mmol) α,α'-azodiisobutyramidine dihydrochloride and 15.9 g (0.14 mol) cysteaminhydrochloride in 300 ml of water. The clear and slightly yellowish solution is acidified with a few drops of hydrochloric acid (32%) to pH 3. The stirred acidic solution is evacuated to 50 mbar and filled with argon. This is repeated three times. With a constant stream of argon, this solution is poured into a 500 ml dropping funnel which is put onto an 'flow-through-reactor' consisting of an 1000ml three-necked round-bottom flask, reflux condenser, thermometer, magnetic stirrer and a 30 cm Liebig-condenser, which is filled with glass wool. The whole apparatus is constantly purged with argon. The dropping funnel is put onto the Liebig condenser, which is heated to 65°C. The flask is heated to 60°C. The solution is slowly dropped through the Liebig–condenser into the stirred flask. This takes 2 hrs. During this time the temperature in the flask is kept between 58-65°C. After the completed addition, the solution is stirred for 2 hrs at 60°C.

NaOH is added to the clear and slightly yellowish solution until pH 10 is reached. The product is purified through reverse osmosis, using Millipore cartridge with a cut-off at 1000 Da and then freeze-dried for 18 hrs. A bright-white solid product is obtained (NH_2 0.70mEq/g, sulfur-value of the elemental analysis (0.73mEq/g; M_n 1350 Da).

Example C-3: N,N-dimethylacrylamide telomer (Mn 1850) synthesis

A 2000 mL round bottom flask is charged with a solution of 198.2 g (2 mol) N,N-dimethylacrylamide (DMA, 2.72 g (10 mmol)) α,α'-azodiisobutyramidine dihydrochloride and 24.8 g (0.22 mol) cysteamine hydrochloride in 600 ml of water.

The clear and slightly yellowish solution is acidified with a few drops of hydrochloric acid to pH3. The stirred acidic solution is evacuated to 50 mbar and filled with argon. This is repeated three times.

With a constant stream of Argon, this solution is poured into a 1000 ml dropping funnel which is put onto an 'flow-through-reactor' consisting of an 1000ml three-necked round-bottom flask, reflux condenser, thermometer, magnetic stirrer and a 30 cm Liebig-condenser, which is filled with glass wool. The whole apparatus is constantly purged with Argon.

The dropping funnel is put onto the Liebig condenser, which is heated to 60°C. The flask is also heated to 60°C. The solution is slowly dropped through the Liebig–condenser into the

stirred flask. This takes about 2.5 hrs. During this time the temperature in the flask is kept between 58-65°C. After the completed addition, the solution is stirred for 2hrs at 60°C. 30 % NaOH solution is added to the clear and slightly yellowish solution until pH 10 is reached. The product is purified through reverse osmosis, using Millipore cartridge with a cut-off at 1000 Da and freeze-dried. A bright-white solid product is obtained. The concentration of amino groups is determined via functional group titration (0.54mEq/g). M_n ~1850 g/Mol.

Example D-1: Preparation of IEM-functionalized acrylamide telomer solution

7.5 g of acrylamide telomer with amino end group (amine titration = 0.70 mEq/g), prepared by Example C-2 are dissolved in 80 ml of HPLC water. Argon is then let to bubble through the solution for the period of about 30 minutes. This mixture is then added to the equimolar amount (0.81 g) of isocyanatoethyl methacrylate (IEM, isocyanate titration = 6.45 mEq/g) under stirring. The whole mixture is then stirred under argon flow for 12 hours. After adding of 0.8 g of NaCl to the solution and 10 minutes stirring, the mixture is filtered through 0.45 µm Teflon filter, degassed by repeated (3x) evacuation and bubbling with argon in order to remove oxygen and used for photografting.

Example D-2 : Preparation of IEM-functionalized DMA telomer solution

15 g of DMA telomer with amino end group (amine titration = 0.54 mEq/g) from Example C-3 are dissolved in 100 ml of HPLC water. Argon is then let to bubble through the solution for the period of about 30 minutes. This mixture is then added to the equimolar amount (1.25 g) of IEM (isocyanate titration = 6.45 mEq/g) under stirring. The whole mixture is then stirred under argon flow for 12 hours. After adding of 1.0 g of NaCl to the solution and 10 minutes stirring, the mixture is filtered through 0.45 µm Teflon filter, degassed with nitrogen in order to remove oxygen and used for photografting.

Examples E-1 – E-4: Photografting of IEM-functionalized acrylamide telomers onto a contact lens surface

1 ml of the IEM-functionalized acrylamide telomer solution from Example D-1 is introduced into small Petri dishes each of a volume of about 2 ml in a glove box. The dried lenses from Examples B-1 – B-4, carrying covalently linked photoinitiator molecules on its surface, are then placed each into one such dish and an additional 0.5 ml of the degassed solution is

added on the lens in order to cover the whole lens with the solution. After 10 minutes, the Petri dishes carrying a lens in the solution are exposed to 14.5 mW/cm^2 ultraviolet light for a period of about 1.5 minutes.

The modified lenses are then withdrawn from the solution, washed twice in destilled water, continuously extracted in ultra pure water for 16 h, autoclaved for 30 minutes ar 121°C and analyzed by AFM, ATR-FTIR and contact angle measurements.

Lens from Example	Dynamic contact angle advancing/receding	Thickness (AFM)
B-1	30° / 0°	40 nm
B-2	0° / 0°	500 nm
B-3	0° / 0°	300 nm
B-4	0° / 0°	370 nm

Example E-5: Photografting of IEM-functionalized acrylamide telomers onto the contact lens surface under ambient conditions

In a laminar flow hood, 1 ml of the IEM-functionalized acrylamide telomer solution from Example D-1 is introduced into a small Petri dish of a volume of about 2 ml. The dried lens from Example B-1, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 0.5 ml of the degassed solution is added on the lens in order to cover the whole lens with the solution. After 10 minutes, the Petri dish with the lens in the solution is exposed to 2.05 mW/cm^2 ultraviolet light (MACAM-UV-Lamp) for a period of 2.5 minutes. The modified lens is then withdrawn from the solution, washed twice in destilled water, continuously extracted in ultra pure water for 16 h and analyzed by AFM, ATR-FTIR and contact angle measurements.

The thickness of the coating is in the range of 350-400 nm as determined by AFM.

Water/air contact angles on the modified lens are 0° adv., 0° rec., 0° hysteresis. In comparison, the contact angles of non-modified lens are 101° adv., 64° rec., 37° hysteresis. The lens holds a continuous water layer on the surface for over 1 minute.

Example E-6 : Photografting of IEM-functionalized DMA telomers onto the lens surface

1 ml of the IEM-functionalized N,N-dimethylacrylamide telomer solution from Example D-2 is introduced into a small Petri dish of a volume of about 2 ml in a glove box. The dried lens

from Example B-1, carrying covalently linked photoinitiator molecules on its surface, is then placed into this solution and an additional 0.5 ml of the degassed solution is added on the lens in order to cover the whole lens with the solution. After 10 minutes, the Petri dish with the lens in the solution is exposed to 14.5 mW/cm^2 ultraviolet light for a period of about 1.5 minutes. The lens is then turned over and the exposition is repeated by applying 14.5 mW/cm^2 UV light for an additional 1.5 minutes.

The modified lens is then withdrawn from the solution, washed twice in destilled water, continuously extracted in ultra pure water for 16 h and analyzed by AFM, ATR-FTIR and contact angle measurements.

The thickness of the coating is in the range of 400-450 nm as determined by AFM.

Water/air contact angles on the modified lens are 14° adv., 9° rec., 5° hysteresis. In comparison, the contact angles of non-modified lens are 101° adv., 64° rec., 37° hysteresis.

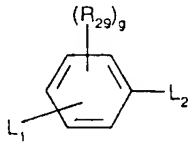
Example E-7: Photografting of IEM-functionalized acrylamide telomers onto the contact lens surface

The contact lenses of Example B-9 are photografted in an aqueous solution according to the method described in Example E-1 using the polyacrylamide macromonomer of Example D-1. Dynamic contact angles of the lenses are: advancing 0°/ receding 0°.

Claims:

1. A process for coating a material surface comprising the steps of:

(a) reacting the material surface with a compound of formula



(1),

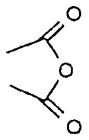
wherein R_{29} is C_1-C_4-alkyl, C_1-C_4-alkoxy, hydroxy, sulfo, nitro, trifluoromethyl or halogen,

g is an integer from 0 to 2,

L_1 is a group, which functions as a triggerable precursor for carbene, nitrene or benzhydrol formation,

L_2 is amino, C_1-C_4-alkylamino, hydroxy, glycidyl, carboxy or a derivative thereof, isocyanato or isothiocyanato, or is a radical of formula

$$- [L_3]_h - (\text{spacer}) - L_2' \qquad (1a), \text{ or}$$

L_2 and R_{29} together form an anhydride radical  ;

L_2' is amino, C_1-C_4-alkylamino, hydroxy, carboxy or a derivative thereof, isocyanato, isothiocyanato, -O-glycidyl or $-O-C(O)-(CH_2)_{h1}-X_2$, wherein h1 is from 1 to 4 and X_2 is carboxy or a derivative thereof,

L_3 is –NH-, $-NC_1$-C_6-alkyl-, –O-, -C(O)O-, -C(O)NH-, -NHC(O)NH-, –NHC(O)O-or -OC(O)NH-;

(spacer) is linear or branched C_1-C_{200}-alkylene which may be substituted by hydroxy and/or interrupted by –O- except for C_1-alkyl, or is C_3-C_8-cycloalkylene, C_3-C_8-cycloalkylene-C_1-C_6-alkylene, C_3-C_8-cycloalkylene-C_1-C_2-alkylene-C_3-C_8-cycloalkylene or C_1-C_6-alkylene-C_3-C_8-cycloalkylene-C_1-C_6-alkylene; and

h is the number 0 or 1;

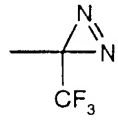
(b) reacting the so modified surface with a functional polymerization initiator having a functional group that is co-reactive to L_2 or L_2'; and

(c) applying one or more different ethylenically unsaturated hydrophilic monomers or macromonomers to the bulk material surface obtainable according to step (b) and

polymerizing said monomers or macromonomers, thereby providing a surface coating onto the material surface.

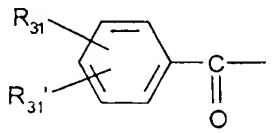
2. A process according to claim 1, wherein the material surface is the surface of a biomedical device, particularly a contact lens, intraocular lens or artificial cornea.

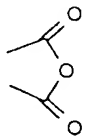
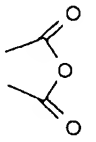
3. A process according to claim 1 or 2, wherein step (a) comprises applying the compound of formula (1) to the material surface and fixing said compound of formula (1) onto the material surface using radiation, in particular UV or visible light.

4. A process according to any one of claims 1 to 3, wherein L_1 is the radical of formula  , g is 0, and L_2 is carboxy or a derivative thereof or is a radical of formula $-L_3$-(spacer)-L_2', wherein L_3 is –C(O)O- or –C(O)NH-, (spacer) is linear C_2-C_{12}-alkylene or –(C_2-C_3-alkylene)-O-$(CH_2CH_2O)_{18\text{-}160}$-($C_2$-$C_3$-alkylene)-, and L_2' is carboxy, a carboxy derivative or a radical -O-C(O)-$(CH_2)_2$-X_2, wherein X_2 is carboxy or a carboxy derivative.

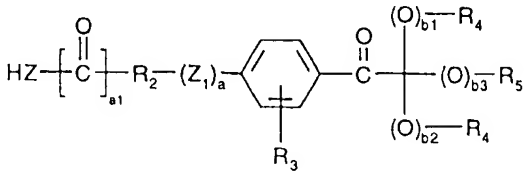
5. A process according to any one of claims 1 to 3, wherein L_1 is the azide radical $-N_3$, g is 0 or 1, R_{29} is methyl, methoxy, hydroxy or nitro, and L_2 is amino, carboxy, a carboxy derivative, isocyanato, isothiocyanato or a radical of formula $-L_3$-(spacer)-L_2', wherein L_3 is -NH- –C(O)O- or –C(O)NH-, (spacer) is linear C_2-C_{12}-alkylene or –(C_2-C_3-alkylene)-O-$(CH_2CH_2O)_{18\text{-}160}$-($C_2$-$C_3$-alkylene)-, and L_2' is carboxy, a carboxy derivative or a radical -O-C(O)-$(CH_2)_2$-X_2, wherein X_2 is carboxy or a carboxy derivative.

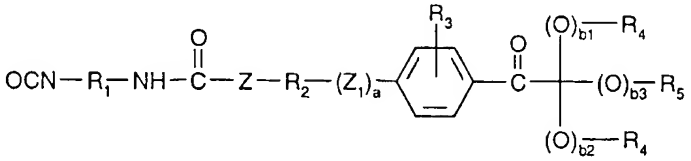
6. A process according to any one of claims 1 to 3, wherein L_1 is a radical of formula

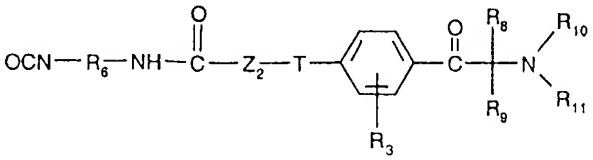
 (2c),

wherein R_{31} is hydrogen and R_{31}' is hydrogen or amino , or R_{31} and R_{31}' together are an anhydride radical  , and L_2 is amino, g is 0 or 1 and R_{29} is amino, or L_2 and R_{29} together are a radical  .

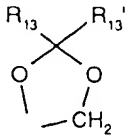
7. A process according to any one of claims 1 to 6, wherein the polymerization initiator according to step (b) is a photoinitiator of formula

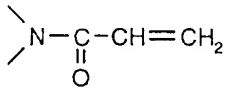
 (3a),

 (3b), or

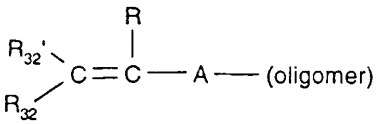
 (3c),

wherein Z is bivalent -O-, -NH- or $-NR_{12}-$; Z_1 is -O-, -O-(O)C-, -C(O)-O- or -O-C(O)-O-; R_3 is H, C_1-C_{12}-alkyl, C_1-C_{12}-alkoxy or N-C_1-C_{12}-alkylamino; R_4 and R_5 are each independently of the other H, linear or branched C_1-C_8-alkyl, C_1-C_8-hydroxyalkyl or C_6-C_{10}-aryl, or the groups R_4-$(O)_{b1}$- and R_4-$(O)_{b2}$- together are $-(CH_2)_c-$ wherein c is an integer from 3 to 5, or the groups R_4-$(O)_{b1}$-, R_4-$(O)_{b2}$- and R_5-$(O_1)_{b3}$- together are a radical of the formula



; R_2 is a direct bond or linear or branched C_1-C_8-alkylene that is unsubstituted or substituted by -OH and/or is uninterrupted or interrupted by one or more groups -O-, -O-C(O)- or -O-C(O)-O-; R_1 is branched C_3-C_{18}-alkylene, unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_6-C_{10}-arylene, or unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_7-C_{18}-aralkylene, unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_3-C_8-cycloalkylene, unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_3-C_8-cycloalkylene-C_yH_{2y}- or unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted -C_yH_{2y}-(C_3-C_8-cycloalkylene)-C_yH_{2y}- wherein y is an integer from 1 to 6; R_6 independently has the same definitions as R_1 or is linear C_3-C_{18}-alkylene; R_{12} is linear or branched C_1-C_6-alkyl; T is bivalent -O-, -NH-, -S-, C_1-C_8-alkylene or  ; Z_2 is a direct bond or -O-$(CH_2)_d$- or –$(OCH_2CH_2)_d$- wherein d is an integer from 1 to 6 and the terminal CH_2 group of which is each linked to the adjacent T in formula (3c); R_8 is linear or branched C_1-C_8-alkyl, C_2-C_8-alkenyl or C_6-C_{10}-aryl-C_1-C_8-alkyl; R_9 independently of R_8 has the same definitions as R_8 or is C_6-C_{10}-aryl, or R_8 and R_9 together are -$(CH_2)_e$- wherein e is an integer from 2 to 6; R_{10} and R_{11} are each independently of the other linear or branched C_1-C_8-alkyl that may be substituted by C_1-C_4-alkoxy, or C_6-C_{10}-aryl-C_1-C_8-alkyl or C_2-C_8-alkenyl; or R_{10} and R_{11} together are -$(CH_2)_{f1}$-Z_3-$(CH_2)_{f2}$- wherein Z_3 is a direct bond, -O-, -S- or -NR_7-, and R_7 is H or C_1-C_8-alkyl and f1 and f2 are each independently of the other an integer from 2 to 4; R_{13} and R_{13}' are each independently of the other H, C_1-C_8-alkyl, C_3-C_8-cycloalkyl, benzyl or phenyl; and a, a1, b1, b2 and b3 are each independently of the other 0 or 1; subject to the provisos that b1 and b2 are each 0 when R_{15} is H; that the total of (b1+b2+b3) is not exceeding 2; and that a is 0 when R_{12} is a direct bond.

8. A process according to any one of claims 1 to 7, wherein a macromonomer of formula



(4),

is applied in step (c),

wherein R_{32} is hydrogen, C_1-C_6-alkyl or a radical -COOR';

R, R' and R_{32}' are each independently of the other hydrogen or C_1-C_6-alkyl;

A is a direct bond or is a radical of formula

$$-C(O)-(A_1)_n-X- \quad (5a) \text{ or}$$

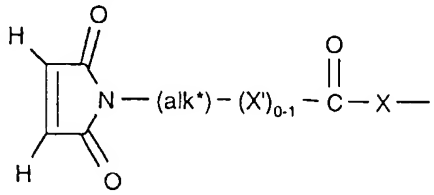
$$-(A_2)_m-NH-C(O)-X- \quad (5b); \text{ or}$$

$$-(A_2)_m-X-C(O)- \quad (5c); \text{ or}$$

$$-C(O)-NH-C(O)-X- \quad (5d); \text{ or}$$

$$-C(O)-X_1-(alk^*)-X-C(O)- \quad (5e); \text{ or}$$

A and R_{32}, together with the adjacent double bond, are a radical of formula



(5f),

A_1 is -O-C_2-C_{12}-alkylene which is unsubstituted or substituted by hydroxy, or is -O-C_2-C_{12}-alkylene-NH-C(O)- or -O-C_2-C_{12}-alkylene-O-C(O)-NH-R_{33}-NH-C(O)- or –NH-(Alk*)-C(O)-, wherein (Alk*) is C_1-C_6-alkylene and R_{33} is linear or branched C_1-C_{18}-alkylene or unsubstituted or C_1-C_4-alkyl- or C_1-C_4-alkoxy-substituted C_6-C_{10}-arylene, C_7-C_{18}-aralkylene, C_6-C_{10}-arylene-C_1-C_2-alkylene-C_6-C_{10}-arylene, C_3-C_8-cycloalkylene, C_3-C_8-cycloalkylene-C_1-C_6-alkylene, C_3-C_8-cycloalkylene-C_1-C_2-alkylene-C_3-C_8-cycloalkylene or C_1-C_6-alkylene-C_3-C_8-cycloalkylene-C_1-C_6-alkylene ;

A_2 is C_1-C_8-alkylene; phenylene or benzylene;

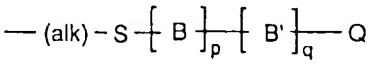
m and n are each independently of the other the number 0 or 1;

X, X_1 and X' are each independently of the other a bivalent group -O- or -NR", wherein R" is hydrogen or C_1-C_6-alkyl;

(alk*) is C_2-C_{12}-alkylene;

and (oligomer) denotes

(i) the radical of a telomer of formula



(6a),

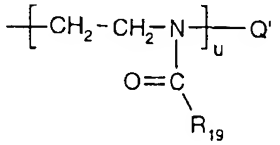
wherein (alk) is C_2-C_{12}-alkylene,

Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator,

p and q are each independently of another an integer from 0 to 350, wherein the total of (p+q) is an integer from 2 to 350,

and B and B' are each independently of the other a 1,2-ethylene radical derivable from a copolymerizable vinyl monomer by replacing the vinylic double bond by a single bond, at least one of the radicals B and B' being substituted by a hydrophilic substituent; or

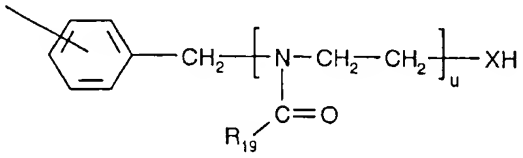
(ii) the radical of an oligomer of the formula



(6b),

wherein R_{19} is hydrogen or unsubstituted or hydroxy-substituted C_1-C_{12}-alkyl, u is an integer from 2 to 250 and Q' is a radical of a polymerization initiator; or

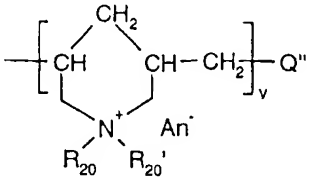
(iii) the radical of formula



(6b'),

wherein R_{19}, X and u are as defined above, or

(iv) the radical of an oligomer of formula



(6c),

wherein R_{20} and R_{20}' are each independently C_1-C_4-alkyl, An^- is an anion, v is an integer from 2 to 250, and Q" is a monovalent group that is suitable to act as a polymerization chain-reaction terminator; or

(v) the radical of an oligopeptide of formula

$$-(CHR_{21}\text{-}C(O)\text{-}NH)_t\text{-}CHR_{21}\text{-}COOH \quad (6d) \text{ or}$$

$$-CHR_{21}\text{-}(NH\text{-}C(O)\text{-}CHR_{21})_t\text{-}NH_2 \quad (6d'),$$

wherein R_{21} is hydrogen or C_1-C_4-alkyl which is unsubstituted or substituted by hydroxy, carboxy, carbamoyl, amino, phenyl, o-, m- or p-hydroxyphenyl, imidazolyl, indolyl or a radical -NH-C(=NH)-NH_2 and t is an integer from 2 to 250, or the radical of an oligopeptide based on proline or hydroxyproline; or

(vi) the radical of a polyalkylene oxide of formula

$$-(alk^{\cdot\cdot}\text{-}O)_z\text{-}[CH_2\text{-}CH_2\text{-}O]_r\text{-}[CH_2\text{-}CH(CH_3)\text{-}O]_s\text{-}R_{34} \quad (6e),$$

wherein R_{34} is hydrogen or C_1-C_{24}-alkyl, (alk") is C_2-C_4-alkylene, z is 0 or 1, r and s are each independently an integer from 0 to 250 and the total of (r+s) is from 2 to 250; or

(vii) the radical of an oligosaccharide;

subject to the provisos that

A is not a direct bond if (oligomer) is a radical of formula (6a);

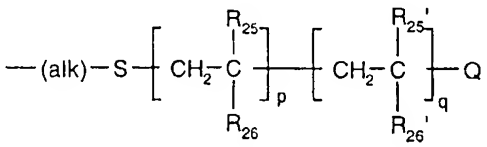
A is a radical of formula (5a), (5b) or (5d) or A and R_{32}, together with the adjacent double bond, are a radical of formula (5f) if (oligomer) is a radical of formula (6b), (6c), (6d) or (6e) or is the radical of an oligosaccharide;

A is a direct bond if (oligomer) is a radical of formula (6b'); and

A is a radical of formula (5c) or (5e) if (oligomer) is a radical of formula (6d').

9. A process according to claim 8, wherein R is hydrogen or methyl, R_{32} and R_{32}' are each hydrogen, A is a radical of the formula (5a) and (oligomer) is a radical of formula (6a).

10. A process according to claim 8 or 9, wherein (oligomer) is a radical of formula

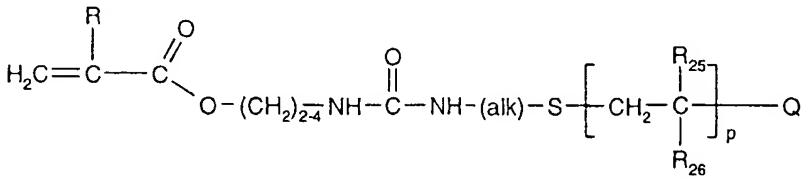


(6a'),

wherein (alk) is C_2-C_4-alkylene, R_{25} and R_{25}' are each independently hydrogen or methyl, Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, p and q are each independently an integer from 0 to 100 wherein the total of (p+q) is an integer from 5 to 100, and R_{26} and R_{26}' are each independently a radical -COOY, wherein Y is C_1-C_2-alkyl, C_2-C_3-alkyl, which is substituted by hydroxy, amino or N,N-di-C_1-C_2-alkyl-amino, or is a radical -C_2-C_4-alkylene-NH-C(O)-O-G wherein -O-G is the radical of trehalose; a radical -CO-NY_1Y_2, wherein Y_1 and Y_2 are each independently of the other hydrogen or C_1-C_2-alkyl which is unsubstituted or substituted by hydroxy, or Y_1 and Y_2 together with the adjacent N-atom form a N-C_1-C_2-alkylpiperazino or morpholino ring; a heterocyclic radical selected from the group consisting of N-pyrrolidonyl, 2- or 4-pyridinyl, 2-methylpyridin-5-yl, 2-, 3- oder 4-hydroxypyridinyl, N-ε-caprolactamyl, N-imidazolyl, 2-methylimidazol-1-yl, N-morpholinyl and 4-N-methylpiperazin-1-yl; -COOH; -SO_3H; o-, m- or p-sulfophenyl; o-, m- or p-sulfomethylphenyl; a radical -$CONY_5Y_6$ wherein Y_5 is C_2-C_4-alkyl substituted by sulfo, and Y_6 is hydrogen; C_1-C_4-alkyl which is substituted by -$NR_{23}R_{23}'R_{23}"^+An^-$ wherein R_{23}, R_{23}' and R_{23}" are each independently of another hydrogen or C_1-C_4-alkyl and An^- is an anion; a

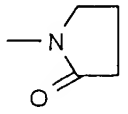
radical -C(O)OY$_7$ wherein Y$_7$ is C$_2$-C$_4$-alkyl, which is substituted by -NR$_{23}$R$_{23}$'R$_{23}$"$^+$An$^-$ and is further unsubstituted or substituted by hydroxy, wherein R$_{23}$, R$_{23}$', R$_{23}$" and $^+$An$^-$ are as defined; and a radical -C(O)O-CH$_2$-CH(OY$_8$)-CH$_2$-O-PO$_2^-$-(CH$_2$)$_2$-N(CH$_3$)$_3^+$, wherein Y$_8$ is hydrogen or the acyl radical of a higher fatty acid.

11. A process according to any one of claims 1 to 10, wherein in step (c) a macromonomer of formula



(4b),

is applied, wherein R is hydrogen or methyl, (alk) is C$_2$-C$_4$-alkylene, R$_{25}$ is hydrogen or methyl, p is an integer of 5 to 50, Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, and R$_{26}$ is a radical

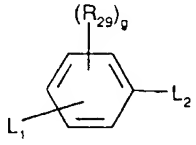
-CONH$_2$, -CON(CH$_3$)$_2$ or  .

12. A composite material obtainable by the process of any one of claims 1 to 11.

13. A composite material according to claim 12, which is a biomedical device, preferably an ophthalmic device such as a contact lens, intraocular lens or artificial cornea.

14. Use of a composite material according to claim 12 for the manufacture of an ophthalmic device, particularly for the manufacture of a contact lens, intraocular lens or artificial cornea.

15. A process for coating a material surface comprising the steps of:
(a) reacting the material surface with a compound of formula

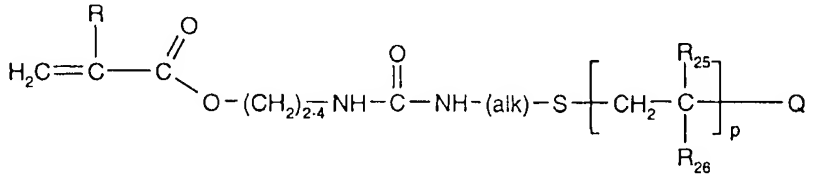


(1),

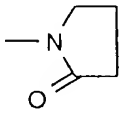
wherein g is 0 or 1, R_{29} is methyl, methoxy, hydroxy or nitro, L_1 is the azide radical $-N_3$, and L_2 is amino, carboxy, a carboxy derivative, isocyanato or isothiocyanato;

(b) reacting the so modified surface with a functional polymerization initiator having a functional group that is co-reactive to L_2; and

(c) applying a hydrophilic macromonomer of the formula



(4b),

wherein R and R_{25} are each independently hydrogen or methyl, (alk) is 1,2-ethylene, R_{26} is $-CONH_2$, $-CON(CH_3)_2$ or  , p is an integer of from 5 to 250, and Q is a monovalent group that is suitable to act as a polymerization chain-reaction terminator, to the bulk material surface obtainable according to step (b) and polymerizing said macromonomer, thereby providing a surface coating onto the material surface.

16. A process according to claim 15, wherein the material surface is the surface of a biomedical device, in particular of a contact lens, intraocular lens or artificial cornea.

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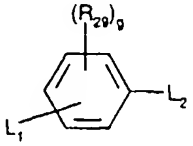
WO 02/032590 A3

(54) Title: PROCESS FOR COATING A MATERIAL SURFACE



(1)

(57) Abstract: The invention relates to a process for coating a material surface comprising the steps of: (a) reacting the material surface with a compound of formula (1), wherein the variables are as defined in the claims; (b) reacting the so modified surface with a functional polymerization initiator having a functional group that is co-reactive to L_2 or L_2'; and (c) applying one or more different ethylenically unsaturated hydrophilic monomers or macromonomers to the bulk material surface obtainable according to step (b) and polymerizing said macromonomers, thereby providing a preferably hydrophilic surface coating onto the material surface. Composite materials obtainable according to the process of the invention have desirable characteristics regarding adherence to the substrate, durability, hydropholicity, wettability, biocompatibility and permeability and are thus useful for the manufacture of biomedical articles such as ophthalmic devices.

INTERNATIONAL SEARCH REPORT

Int...nal Application No
PCT/EP 01/11883

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B05D1/18 B05D3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B05D G02B C08J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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[X] Further documents are listed in the continuation of box C.

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3 June 2002	10/06/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Slembrouck, I

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A	WO 96 20919 A (CIBA GEIGY AG ;CHABRECEK PETER (CH); DIETLIKER KURT (CH); LOHMANN) 11 July 1996 (1996-07-11) cited in the application claims 39-41; examples	1,12,14, 15
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